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Physical Exercise Ameliorates Symptoms of Anxiety and Depression

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Regular physical exercise invariably promotes structural and functional integrity in the brain and body, whether or not it is engaged upon for the maintenance of accustomed health condition or acceded to under pressures of an unhealthy or diseased condition. The improvement and resilience of functional and biomarker expressions during ageing, cellular senescence and immunosenescence, the alleviation of deficits in cognitive performance through the optimal augmentation of cerebral plasticity and the enrichment of individuals' proclivities for advantageous ontogenetic and epigenetic dispositions are benefits accruing from a lifestyle built around routine activity [1-3] whereas a sedentary lifestyle promotes debility [4]. The notion of 'organismal robustness', through which 'dormant', or otherwise, genetic predispositions will translate into disease in individuals with decreased organismal robustness [5,6], offers a growing, as yet underestimated, preventative/interventional characteristics that describe the decelerating ageing-related debilities and is bolstered by the concomitant aspect of 'organismal resilience'; regular exercise/activity has been shown to offer consistent benefit for maximizing organismal resilience against a broad range of extrinsic and intrinsic stressors, such as infections, injury/surgery, wound-healing, toxicants, genetic predispositions and frailty [7,8,9]. Thus, the capacity of acute exercise to promote cortical resilience-the ability to recover from temporary perturbation, active cTBS to the left dorsolateral prefrontal cortex, through applications of moderate-intensity exercise and very light-intensity exercise has demonstrated neuroprotective, resilience-promoting effects of exercise [10]. Exercise has brought about beneficial influences upon neurocognitive, including executive function and working memory, emotional, including self-esteem and depressed mood, motivational, including anhedonia and psychomotor retardation, and somatic domains, including sleep disturbances and chronic aches and pains [11]. A variety of associated biomarkers, such as a chronically dysregulated hypothalamic-pituitary-adrenal (HPA) axis, anti-neurodegenerative effects, monoamine metabolism regulation and neuroimmune function are ameliorated through adherence to exercise regimes. In female rats subjected to restraint stress, voluntary running behavior effectively reduced stress-induced corticosterone, but not anxiety, in estrogen-administered animals [12].

Several physical health benefits are conferred by regular physical exercise in primary prevention, treatment and rehabilitation for many chronic diseases (e.g. cardiovascular disease, diabetes, cancer, etc) in addition to premature mortality [13-14]. Exercise is associated firmly with lasting improvements in mental and somatic health and psychological well-being [15-16], and as Boreham and Riddoch [17] have indicated: "from the cradle to the grave, regular physical activity appears to be an essential ingredient for human well-being" (p. 24). Ten percent reductions in the rate of adult Canadians presenting neuropsychiatric disorder sedentary behavior would give fewer167,000 cases of common mental disorders, a 25% reduction would result in 389,000 fewer cases [18] with greater beneficial for male patients. Physical inactivity was a significant risk factor for common mental disorders with approximately 780,000 cases nationally attributable. The advantages of physical exercise over pharmaceutical and other more-or-less approaches, such as antidepressant drugs, as an intervention for anxiety depressive conditions are numerous in comparison with traditional treatments: (1) exercise improves the general physical health status (e.g. increased oxygen uptake, decreased blood pressure, and reduced risk for coronary diseases). (2) Exercise provides a number of benefits in neurocognitive domains [19]. (3) Physical exercise alleviates the effects of stress and expressions of negative affect and elevates psychological well-being and health [20,21]. (iv) It has been established that the dysregulation of neuro-immune functions may contribute to depressive states [22,23], the unique role of exercise specifically [24] and generally in this regard [25] ought to be noted. (v) In terms of 'cost-benefit', it is likely that exercise group interventions (often employer-subventioned) ought to be more cost-efficient than individual psychotherapy or drug therapy. (vii) Exercise regimes may be considered also in terms of behavioural schedules whereby the intervention compliance ought to be reinforced through application of the 'schedule-induced behaviour principle'. (viii) Compared with psychotherapy or drug therapy, stigmatizing considerations are absent with exercise regimes. (ix) Both the psychomotor retardation and anhedonia symptom profiles associated with deficits in dopaminergic systems; it has been shown that physical exercise ameliorates both functional, biomarker and quality-of-life aspects [26-28]. (x) Finally, although physical exercise assumes no direct side-effects compared with traditional antidepressant medication, there exist real risks that individuals with depressive tendencies undergoing depressive episodes may 'abuse' varieties of exercise for the purpose of mood-elevation [29].

Physical exercise offers protective influences against stress-induced anxiety and depressiveness in laboratory rodents. Individuals with vulnerability for anxiety, depressive states and posttraumatic stress disorder present conditions are all rendered resilient through the intervention of physical exercise schedules [30-34], as well as affecting positively pain pathways and stress and fear expressions [35-37]. Stress resilience/resistance appears to be independent of exercise controllability concurrent with rendering protection against uncontrollable stress effects on behavior and biomarkers [38,-40]. Activity-traing schedules advance cognitive performance and academic achievement in the prevention of neuropsychiatric disorders through the promotion of neuropsychological and neuroplasticity mechanisms [41-43]. Herrera et al. [44] have demonstrated that both voluntary and forced running by laboratory rats are linked to the rewarding effects of exercise, which though independent of exercise controllability, implicate mesolimbic and striatal dopamine circuits. It has been established persuasively the resilience to psychiatric vulnerability and resistance to injury and neurodegenerative forces are buttressed by such processes as exercise-induced neurogenesis,

angiogenesis and neurorestoration that implicate the involvement of the plasticity endowered by growth factors, particularly brain-derived neurotrophic factor (BDNF) [45-50] while resistance exercise reduces drug self-administration, muscle hypertrophy and BDNF expression in the nucleus accumbens [51,52]. β-hydroxybutyrate, a metabolite which is elevated following prolonged physical exercise, generates the activities of *bdnf* promoters. Sleiman et al. [53] have shown that β-hydroxybutyrate acts upon HDAC2 and HDAC3, histone deacetylases 2 and 3, which in turn affect selective *bdnf* promoters, eventually inducing increased levels of neurotransmitters. Thus, the mechanisms of BDNF generation through exercise seem linked to the epigenetics of exercise [54].

In chronic obstructive pulmonary disease (CPPD), high levels of anxiety and other negative affective states are predictive for disability and mortality [55,56]. Di Marco et al. [57] have argued that the COPD management purpose has the requirement of promoting exercise capacity and daily activity adherence in view of the evidence that these outcomes exert direct effects upon patients' quality-of-life, health co-morbidities (heart and metabolic diseases), and prognosis for well-being. The augmentation of physical exercise ability offers a long-term approach that regulates intrinsic pulmonary and systemic manifestations of this chronic disorder. Nevertheless, one ought to aware of the situation implying that patients presenting COPD need to understand the relationship between the improvement of "potential" exercise capacity and daily physical activity maintains a moderate to weak level. In the application of a pulmonary rehabilitation program incorporating aerobic exercise that implicates a multidisciplinary approach, Catalfo et al. [58] demonstrated improvements in the anxiety and depressive symptoms of COPD patients with particular emphasis additionally upon the reduction of fat mass and BMI selectively in those patients presenting depressiveness. Despite the efficacy of exercise programs in rehabilitation from affective disorder, post-exercise analyses and follow-up studies are necessary both for development and delivery of interventions for patient mental health consumers and assessing the adherence-oriented engagement of clinicians [59-62]. In this context, it may be critical to take notice of findings reporting gender-related differences in the mood-elevating response of acute aerobic exercises whereby healthy female participants, although more likely to report higher levels of anxiety and depressiveness, experienced greater improvements, than males, on fatigue, confusion, energy, total mood disturbance and state anxiety [63].

Vulnerability to emotional regulation disturbances, persistent high levels of negative affect, anxiousness and depressiveness with reports of chronic high stress and low energy may signal individuals' distress on exposure to events that generate negative emotions. This vulnerability may take the form of an inability to mobilize a flexible behavioral repertoire in response to changing emotionally-charged events and circumstances; typically, resilient individuals express emotional flexibility, a major protectant against depressiveness and related affective conditions: a) in response to frequently altering emotional stimuli; and b) across multiple modalities of emotional responding [64,65]. The connections between emotional flexibility, resilience and exercise are complex. Shields et al. [66] studied the relationship of physical activity to negative emotions assessed in real-time during simulated-peer-rejection. They found that the predicted generation of negative emotions in response to peer-rejection and flexible reduction of negative emotions in response to peer-acceptance. Contrastingly, regular aerobic exercise was shown to prevent the onset or deterioration of depressed mood among individuals with limited emotional flexibility [67]. Bernstein and McNally [68] examined the effects of a bout of moderate aerobic exercise upon emotional expressions of young men and women during post-exercise exposure to a sadness-inducing length of film (negative mood induction). The aerobic exercise intervention attenuated the negative emotions in participants who experienced regulatory emotional difficulties. Doubtlessly, in a lifestyle deprived of motor activity and exercise, sedentary existence is associated with affective disorder, including anxiety, depressiveness and poor quality-of-life [69-76].

Both as a major therapeutic intervention and as an adjunctive therapy, physical exercise has demonstrated reliable efficacy for mild-to-moderate depression, with or without anxiety [77-83]. Greer et al. [84] assessed psychosocial functioning in patients presenting non-remitted major depressive disorder. They observed that participants expressed marked improvements in functioning across all the domains examined: work, social adjustment, health quality, quality-of-life and enjoyment and satisfaction. The authors imply that exercise offers an important augmentation therapy adjunctive to antidepressant treatment [se also 85]. Nevertheless, taking into account the incidence of anxiety, depression and suicidal thoughts and/or behaviors among adolescents [86, see also 87] with 6 to 10% of these individuals meeting criteria for disorder and 32% describing suicidal thoughts [88-90], it is a matter of some concern that 80% of younger adolescents (early teenagers 13-15 years) show inadequate and lack of adherence to exercise-activity [91-93]. Among university students, sports activity involving tennis exercise reduced anxiety and depressive symptoms and enhanced well-being [94]. McMahon et al. [95] observed that frequency of exercise activity was correlated positively with well-being and correlated negatively with both anxiety and depressive symptoms, reaching up to a threshold of moderate frequency of activity. Using a multi-level mixed effects model, they obtained greater frequent physical activity and participation in sports that contributed independently to higher levels of well-being and lower levels of anxiety and depressive symptoms over both genders. It is emphasized that elevated activity levels and sports participation among the least active juveniles ought to be developed in community and school-based interventions to promote well-being. In Law students that reported high levels of distress, a strong negative correlation between

exercise propensity and psychological distress [96]. Similarly, in young adults presenting nonsuicidal self-injurious behavior were markedly less likely or never engaged in exercise activity before entering the partial hospital program [97]. In osteoarthritic patients marked associations between exercise outcome expectations, self-efficacy and depression were registered [98].

Several correlational analysis studies show that exercise is negatively related to anxiety-depressive symptoms in the elderly, postpartum women and cancer and other patient groups [e.g. 99-106]. Also, a number of prospective longitudinal and dose-response studies have found that regular exercise at baseline is related to lower risk for subsequent depression [107- 109], although the relationship between exercise and depression across time may be best viewed as reciprocal [110]. Moreover, a considerably large number of intervention studies have by now investigated the effect of various exercise programs on depression and the vast majority of them indicate that exercise significantly reduces depression [e.g. 98,110,111]. In addition to cross-sectional and/or longitudinal studies, a number of meta-analyses of intervention studies have been published during the last 20 years [112-116]. Under conditions of prolonged physical inactivity psychological, affective, status tended to deteriorate [117]. Both resilience and social support mediated the effects of exercise [118]. The effectiveness of exercise for improvement of symptoms among patients presenting major depression provides expectations for non-invasive interventions for these patients [119]; they have presented also practical suggestions for helping patients initiate and maintain exercise in their daily lives. Taken together, the major findings from eight meta-analyses so far show that exercise has an antidepressant effect compared to control conditions that ranges from slightly moderate (g = -0.40) [120] to very large (g = -1.39) [121]. Furthermore, exercise programs improved clinical symptoms, global functioning, quality-of-life and depressive symptoms in schizophrenic patients [122-124].

In conclusion, several conditions of psychological and somatic illness present co-morbidities referring to affective dysregulation, most commonly anxiety, depressiveness, alcohol and substance abuse, suicidal behaviour and ideation and loss of cognitive flexibility. The present treatise discusses the influences of physical activity in alleviating both the symptoms and concurrent biomarkers of disorder while improving resilience, emotional flexibility, well-being, cognitive performance, mood and quality-of-life. Nevertheless, the optimal situation under which exercise and activity are arranged requires much further study; in this regard, heart rate variability, a measure of autonomic nervous activity under conditions of duress, was found to be preferentially augmented by combinations of music with exercise [125,126]. Finally, the neuroimmune functioning upsurge from physical exercise as expressed by the anti-inflammatory effect of higher baseline serum IL-6 levels are linked with reduced depressive symptom severity following 12 weeks of exercise [127].

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