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Exercise and mental health

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ABSTRACT – This paper reviews the mood altering properties of exercise and its potential in the prevention and treatment of mental disorders. The role of the brain monoamines, opioid peptides, the sympathetic nervous system, and cognitive behavioural theory as mediating pathways for the psychological benefits of exercise is critically examined. Clinical trials on exercise are reviewed and suggestions are made for future research in this field.

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What are the psychological benefits of exercise? Can an exercise programme be used in the treatment and prevention of mental disorders?

While it is established that regular exercise results in physiological benefits of use in the rehabilitation and prevention of coronary heart disease (1), peripheral vascular disease, mild hypertension or obesity, the benefits to mental health are harder to evaluate and less well documented. Yet, "running therapy" and exercise programmes for minor mental disorders have been enthusiastically embraced in the United States (2) and are creating an upsurge of interest in the United Kingdom. This paper is a review of the theoretical background to this treatment strategy emphasising the mediating pathways between exercise and central neuronal changes.

Immediate effects of exercise

Three main types of exercise exist (3), which focus on:

1. Aerobic endurance.
2. Anaerobic endurance.
3. Flexibility, co-ordination, and relaxation.

Aerobic exercise consists of physical work sustained for long periods (for example distance running or swimming) with training designed to increase the efficiency of the oxygen transport system. Anaerobic exercise involves high intensity work sustained for very short periods (for example weight lifting or

sprinting). Here the training is designed to increase muscular strength. An example of the type of exercise that improves flexibility, co-ordination and relaxation of the muscles is Yoga.

Aerobic or anaerobic exercise are stimulants which lead to physiological arousal of the brain and an increased sympathetic tone. The mood of healthy subjects who exercise *regularly* is altered immediately after a period of vigorous exercise. In the short-term they become less anxious, depressed or angry and may even feel euphoric (4-7). In particular, the level of anxiety gradually returns to the previous state by about the fifth hour after exercise (8). Therefore a lower level of anxiety could theoretically be maintained by exercising at least three times a day. The immediate changes in mood after exercise and the time course of such changes have not been documented in subjects who do not habitually exercise (such as most patients with mood disorders). Such patients have a higher potential for a change in mood, but if they are normally sedentary, a period of training is usually required before much exercise is possible.

During strenuous exercise the cardiac output may increase up to five-fold from about 5 l/min to 25 l/min, which is primarily diverted to the muscles. There is, in addition, up to a two-fold increase in the cerebral blood flow (9). Conversely there is a decreased cerebral blood flow in the grey matter of both hemispheres in depression (10). Regional

cerebral blood flow reflects the level of neural activity and metabolism (11). Thus during exercise in a depressed patient, the neural activity will be increased. However Uytendhoef et al. (12) have reported a more complicated picture of regional blood flow in depression with left frontal hypervascularisation and right posterior hypovascularisation.

Long-term physiological adaptations of aerobic exercise

If exercise is an effective measure for altering mood in the short-term in psychologically healthy persons, could an exercise programme lead to long-term changes in patients with mood disorders? A number of physiological adaptations occur after an aerobic exercise programme which are usually measurable after 6–8 weeks. The usual recommendation is to exercise at 60–70% of the maximal aerobic capacity for a minimum of 20 minutes, three times a week. In general the efficiency of the oxygen transport system is increased by an increased stroke volume and muscle blood flow (13). A smaller increase and a faster recovery to the baseline occurs in the sympathetic activity and several hormonal levels for the same physical workload (9). Psychological stress appears to be handled similarly to a physical workload, fit subjects showing a more adaptive and efficient response than the less fit. For example, Keller (14) randomly allocated 60 subjects to either a 10 week aerobic exercise, or a Yoga meditation or a music appreciation programme. The subjects were tested before and after the programme with a psychological stress such as Raven's progressive matrices or Stroop's colour word test that had to be completed in a limited time. Over the course of the study participants in the exercise programme showed the fastest recovery in 1) the heart rate in response to the same workload, and 2) the electrodermal response when presented with the same psychological stress. This adaptation in sympathetic activity after an exercise programme may have particular relevance for conditions in which the physical symptoms of anxiety are prominent. As an additional benefit it seems that a subject learns to associate the usual physical symptoms of sympathetic activity and hyperventilation with a normal healthy state, rather than with anxiety, thereby interrupting the feedback loop between the physical

sensations and the cognitive appraisal — usually the basis for a panic attack. However, no controlled clinical trials exist for exercise in the management of generalised anxiety states. Orwin has reported cases of agoraphobia (15) and a case of a situational phobia (16) which have been successfully treated by running before exposing the patient to the phobic stimulus. This was replicated by Muller (17) for a case of "elevator phobia" but the approach has not been systematically compared to traditional therapies in a controlled trial.

The hormonal adaptations that occur after regular exercise include those mediated by the hypothalamic-pituitary-adrenal axis. An aerobic exercise programme leads to a smaller increase and faster recovery to the baseline of cortisol levels for the same workload (18) and, by analogy, the same psychological stress. This adaptation may be relevant to the various mental states now found to be associated with hypersecretion of cortisol and non-suppression on a dexamethasone suppression test.

The brain monoamines as the mediator of mood changes

Central monoamine metabolism can be disturbed in clinical depression and in general a sub-group of patients exists with decreased metabolism of either the noradrenergic or serotonergic system. The effect of anti-depressants and ECT is to enhance the activity of the monoamines.

There are serious limitations to the measurements of the acute or long-term changes of central catecholamine or serotonin metabolism with exercise. Plasma or urine 3-methoxy-4-hydroxyphenylglycol (MHPG) can normally be used as a crude index of central noradrenaline degradation (19,20), but the acute increases in circulating catecholamines during exercise from the Adrenal Medulla will grossly contaminate the measurement of plasma MHPG (21). Most data on central monoamine turnover in depression have been obtained by measurements of lumbar cerebro-spinal fluid (CSF) metabolites, and in particular 5-Hydroxyindoleacetic acid (5-HIAA) (22). However, concentrations of lumbar CSF may be weakly correlated with brain monoamine turnover, because the lumbar canal is a cul-de-sac and because many amines are found in the spinal cord and must therefore contribute to the CSF values (23). Acute changes in lumbar CSF

monoamines with exercise have been demonstrated in depressed patients by Post (24) and Fortherby (25). In the former study CSF 5-HIAA and vanillylmandelic acid (VMA) were significantly higher after 4 hours hyperactivity than in the same patients after bed rest.

Animal studies also provide the indirect evidence for acute and long-term changes in brain monoamine turnover (26). For example, Brown (27,28) placed rats on an exercise programme which consisted of 30 min of treadmill running for 5 days a week over 8 weeks. The rats were then sacrificed and the noradrenaline and serotonin brain concentrations were significantly greater in comparison to sedentary controls. This result is of course similar to the overall effect of anti-depressant drugs and ECT (22).

Paradoxically, the evidence that changes in brain monoamines mediate the beneficial effect on mood in exercise, has also been used to refute the primary role for monoamines in the pathophysiology of depression. It suggests that the monoamines mediate a behavioural component of depression, such as underactivity or retardation.

The effect of aerobic exercise on the dopaminergic receptors in the corpus striatum of rats has also been studied (29). Here the animals ran on a treadmill up to 1 hour a day, 6 days a week for 12 weeks. [³H]-spiperone was then used to label the dopamine receptors in the corpus striatum. The exercise group had significantly higher [³H]-spiperone binding compared to sedentary controls. This would suggest an improvement in extra-pyramidal symptoms for patients on neuroleptics as a result of an exercise programme.

In summary, evidence exists for both acute and long-term changes in brain monoamine turnover with exercise. However the significance of similar changes in normal mood states or in mental illness is not yet clear: thus making a monoamine link between exercise and alterations in mood highly speculative.

The opioid peptides

A number of investigators have demonstrated marked elevations of plasma beta-endorphins in response to aerobic exercise (30-36). There is a wide variation in the response of plasma met-enkephalin (36,37) or leu-enkephalin (37,38), but in most sub-

jects the concentrations will rise. The findings of these studies promoted speculation over the role of endorphins in the "runner's" high (39,40) and in exercise dependence (41). However, the experimental evidence to link these phenomena is still lacking. The role of opioid peptides in normal mood states or in mental illness is less clear than the monoamines (42).

There are three main families of opioid peptides, which have different receptor affinities and anatomical distribution. The mu receptor mediates most of the analgesic action, for which morphine is the prototypal agonist and naloxone is the antagonist (43). Kappa and delta receptors have also been identified in the human brain (44), and indirect evidence exists for the presence of epsilon and sigma receptors. The function of each receptor is speculative, and include dysphoria, euphoria and hallucinations (45).

The demonstration of elevated plasma beta-endorphins appears to be a non-specific response to acute stress (46). Plasma beta-endorphin and ACTH are derived from a common precursor in the pituitary, pro-opiomelanocortin, which secretes both hormones in response to the same stress (30). However they are relatively impermeable to the blood-brain barrier except at the hypothalamus and therefore cannot be implicated in the acute changes in mood (47). There may be central changes in opioid peptide levels with exercise, but the evidence for this in human subjects could only be obtained directly from the CSF. Even then it would be difficult to know how altered lumbar CSF levels would reflect changes in discrete areas of the brain and different mood states.

Indirect evidence for central opioid activity can be gained from the use of antagonist drugs or a PET Scan with an opiate labelled ligand (48). To date only antagonist drugs such as naloxone and naltrexone have been used which have preferential affinity for mu receptors and an analgesic function. For example Janal (7) studied 12 long-distance runners on two occasions in a double blind crossover trial. On 1 day they received two intra-venous injections of 0.8mg naloxone at 20 min intervals following a 6 mile run. On the other day they were given 2 equal volume injections of normal saline. Ratings on depression-euphoria and regretful-joyful scales were increased but not until 30 min after completing the run. Ratings of fatigue, anxiety, and

energy were not affected by the run. Under saline treatment ischaemic pain and discriminability of thermal stimuli were reduced post-run. This hypoalgesic effect was equivalent to 10 mg morphine and lasted about 25 min after the run. If beta-endorphin is elevated centrally then it is relatively non-selective and can occupy all three receptor sub-types. The ratings of mood elevation were reversed by naloxone which at 1.6 mg intra-venously was presumably of a sufficiently high dose to antagonise receptors other than the mu.

In a similar study Markoff (6) demonstrated decreased ratings of depression, anxiety, and anger at 15-20 min after 1 hour's running, but 2 x 0.4 mg naloxone sub-cutaneously failed to reverse the changes in mood. Presumably in this experiment the dose was insufficient to antagonise receptors other than the mu. Replication of such trials with specific delta, kappa, epsilon or sigma receptor antagonists is awaited with interest.

Could a training programme enhance the central release of opioid peptides? These neurotransmitters might then be implicated in any long-term change in mood and the phenomenon of exercise dependence in some individuals. Evidence for enhanced secretion of peripheral beta-endorphins was demonstrated by Carr (35), although this study was criticized for retesting subjects after their exercise programme at a higher physical workload (46). Howlett (36) studied 15 normal women during an intensive 8 week exercise programme and failed to replicate the findings of Carr (35). Furthermore, the release of met-enkephalin during exercise was almost abolished by the training programme.

Blake (49) failed to demonstrate any enhancement in central opioid peptide levels in 16 rats after an 8 week training programme compared to 16 sedentary controls. Before sacrifice, one half of each group received a final fatiguing bout of exercise. Regardless of their prior training regime, fatiguing exercise resulted in an acute increase in beta-endorphin content in the nucleus accumbens and leu-enkephalin in the ventral tegmentum. Both areas are part of the limbic system and exogenous administration of opiates in such areas results in analgesia. In addition Pert (50) has demonstrated an increased enkephalin receptor occupancy in the whole brain of rats immediately after 15 min of running on a treadmill.

In summary, experimental evidence exists for acute but not chronic central changes in opioid peptides with exercise. Opiate receptor function is still best confined to analgesia and its role in altered mood states can only be satisfactorily tested when there are more specific receptor antagonists. On theoretical grounds an exercise programme might be useful in the adjunctive treatment of opiate dependence — by substituting the exogenous opioids for the endogenous. However, no controlled trials have been performed.

Psychological explanations of the benefits of exercise

An explanation of the beneficial effects of exercise in accord with psychoanalytical theory might be that exercise provides a "cathartic" function for the discharge of anger and hostility — emotions that are directed toward the self in depression. An alternative interpretation could be that exercise fulfils an adaptive defence mechanism by "sublimation", whereby psychic energy is rechannelled away from the self into a socially acceptable outlet. Such "understanding" of the role of exercise has obvious face value but does not lend itself to experiment.

Cognitive behavioural therapy provides another theoretical framework for depression. The occurrence of repeated intrusive thoughts and cognitive distortions can be construed as primary components of the depressed state. In addition a depressed mood is accompanied by a greater retrieval of negative memories than positive ones (51,52). The dwelling on depressive ideas leads to a depressed mood, and a vicious circle is established. Cognitive therapy aims to change the mood of the subject by altering the maladaptive thinking. One effective procedure taught to patients is distraction, in which the patient forces himself to attend to something other than his or her depressive thoughts (53,54). A common observation amongst runners is that exercise allows their thoughts to drift. Exercise may therefore in the short-term be a means by which subjects allow themselves to be distracted away from depressive thoughts, facilitating the retrieval of positive memories. However, exercise is unlikely to be sufficiently frequent to lead to permanent changes in the postulated maladaptive thinking. Some evidence for a distraction hypothesis in exercise comes from Pennebaker (55) who exer-

cised healthy subjects on a treadmill. Subjects who heard distracting sounds through a pair of headphones reported less fatigue and fewer symptoms than subjects hearing an amplification of their own breathing. The results suggest that increased attention to internal cues results in greater perception of fatigue and physical symptoms.

Self-mastery is conceptualised as the degree to which an individual regards his life as under his own control instead of being fatalistically determined (56). It is possible that subjects in an exercise programme gain a greater sense of mastery and control over their bodies and this may generalise to other areas of their life. For example Sinyor (57) randomly allocated 38 healthy males to either aerobic, anaerobic (weight-lifting) or waiting-list control groups for a 10 week programme. Only measures of self-mastery were significantly increased in the aerobic exercise group after the programme. None of the questionnaires for self-mastery has been validated in a depressed population. Such measures may be influenced by the mood of the subject and may improve when he or she is no longer depressed. It thus becomes tautologous to argue that change in mood occurs through an increased sense of self-mastery.

Lastly, the psychological benefits of exercise programmes may be non-specific. The trials that have been performed so far on exercise in depression have been conducted in small groups and some of the benefits may have occurred as a result of social interaction and group participation. Most groups are conducted about three times a week — resulting in a relatively high degree of attention from a health professional. The non-specific benefits of exercise may be tested in clinical trials by the inclusion of a control group that receives the same degree of attention and social interaction as the exercise group.

Clinical trials with exercise

Exercise programmes in clinical groups have been used predominantly in the treatment of depression. Several studies in the United States (58-63) and in Norway (64), have recently been reviewed by Simons (65). All previous studies have shown positive benefits for an exercise programme but the studies have lacked the rigour of controlled clinical trials. Studies that have focussed on subjects who have no demonstrable psychopathology have failed

to demonstrate any psychological benefits (66-68).

Only two studies (61,64) have selected depressed patients on standardised diagnostic criteria and randomly allocated them to an exercise group or control group. Martinsen (64) randomly allocated 49 in-patients with a DSM III diagnosis of a major depressive episode either to an aerobic exercise programme ($n=28$) or to occupational therapy ($n=21$). Both groups spent an hour with the supervisor three times a week. The aerobic exercise group were significantly less depressed on the Beck depression inventory after 9 weeks. However the small number of subjects led to a bias between the groups at inclusion. Twice as many subjects (66%) in the control group were on anti-depressants compared to the exercise group (33%) which suggests that they were more severely ill and had the worse prognosis. Although the mean Beck scores at inclusion in the trial were 25 (Range 14-37) in the exercise group, and 31 (Range 14-53) in the control group, no statistically significant differences existed between the groups. In the study by Doyno (61), 41 women who met Research Diagnostic Criteria for a depressive episode were randomly allocated to one of three groups: aerobic running, anaerobic weight-training, and a waiting-list control. Both exercise groups met under supervision four times a week for 30 min periods. Depression as measured by the Beck depression inventory and the Hamilton rating scales was significantly reduced in the two training groups with no change in the control group, and this was maintained at 1 month follow-up. There was no difference between the exercise groups.

The number of subjects in all previous studies is far too small, leading to a significant risk of bias between groups before intervention. So far the trials have used only self-report measures for assessment of mood, which also have their limitations. An objective clinical assessment is required, and at follow-up the psychiatrist must be blind as to the group to which a subject has been allocated. There have been no long term follow-up studies. One of the most interesting questions is whether the risk of relapse can be reduced in vulnerable individuals by their remaining in an exercise programme? A high prevalence of a past history of primary affective disorder has been documented in runners by Colt (69). Seven out of a sample of 22 (32%) female runners and six of 39 (15%) male runners received

a diagnosis of a primary affective disorder using the lifetime version of the schedule of affective disorders and schizophrenia. No details are given on the percentage that had improved since they started to run.

Future implications

I have discussed the various mental disorders that might benefit from exercise programmes and for which good controlled trials are required. These include the adjunctive treatment of depression, anxiety states, extra-pyramidal symptoms of neuroleptic medication, and opiate dependence.

There may be important implications for the prevention of minor mental disorders if it can be reliably demonstrated that regular exercise is important for mental health. Community surveys reveal substantial psychiatric morbidity in the form of minor mood changes predominantly of depression and anxiety (70). However, a subject needs a good deal of motivation and self-discipline to comply with a regular exercise programme. Individuals with minor mood disorders usually lack the self-confidence, and clinically depressed subjects will undoubtedly lack the motivation to commence an exercise programme on their own. Therefore a patient will initially nearly always require the support and training of a health professional such as a physiotherapist.

Psychiatric in-patients are less physically fit and more obese than non-institutionalised individuals (71-73), which may be a consequence of the sedation and increased appetite that results from psychotropic medication or may be a facet of the psychiatric disorder itself (for example apathy and motor retardation). Thus for their physical constitution alone such patients would benefit from regular physical activity and this should be more vigorously encouraged.

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