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The Role of Tranquillisers in Sport and Exercise

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1. INTRODUCTION

In recent years the demands of modern society are such that individuals may find themselves increasingly under stress from daily life. These stresses may result in the development of symptoms of anxiety or over-arousal in which the central nervous system (CNS) becomes over-activated. Continued exposure to such stress may cause psychological problems in which an individual becomes hyperactive, neurotic, highly excited or anxious. Anxiety may also be reflected in physiological symptoms such as high blood pressure and hormonal imbalances. Severe personality disorders and / or physical breakdown may result. In an attempt to relieve these symptoms pharmacological manipulation of arousal levels has all too commonly been preferred to behavioural changes, relaxation techniques and avoidance strategies. As a result tranquillising drugs have become the most clinically prescribed drugs of modern times.

Sportspersons may not be immune from similar daily stresses, particularly as they are exposed to the unique demands of high level sport. It is possible that tranquillisers may have a role to play in assisting athletes and sportspeople to meet the psychological demands of top level sport. Firstly, there have been reports of sportspeople prone to pre-competition anxiety employing such drugs as a means of controlling arousal and ensuring sleep prior to competition [1]. Secondly the hypnotic nature of the drugs has led to their use in assisting individuals to adjust to new time-zones after international travel [2]. Thirdly, in certain instances tranquillising agents have muscle relaxant properties and are used to relieve muscle spasms. Such physiological effects may aid the injured athlete who may draw on the drugs for pain relief and rehabilitation from muscle injury. Research has focused on tranquilliser use in clinical and occupational medicine with minimal observations being made in exercise contexts. Clinical and ergonomic situations must therefore be extrapolated to the sporting context to gain insight into the possible roles that the drugs might play in sport and exercise. This paper will explore the potential roles of selected tranquillisers within sport and exercise and also highlight some of the physiological, psychomotor and psychological effects demonstrated by the drugs.

2. PHARMACOLOGY OF SELECTED TRANQUILLISERS

Therapeutically the group of drugs known as tranquillisers are used to treat a wide range of psychological disorders. They are sub-divided according to their different chemical structures and properties and the varying clinical effects that they have. When considering the effects of tranquillisers on performance there is a need to examine the pharmacokinetics of the drugs and their metabolites. The pharmacokinetics of selected tranquillisers have been extensively reviewed elsewhere [3,4].

The group of drugs termed the major tranquillisers are effective in the treatment of excited or agitated psychotic states such as schizophrenia, senility and delirium. They may not, however, be of benefit in the treatment of depression [5]. The mode of action of the major tranquillisers is focused around the branches of the CNS in which dopamine is the neurotransmitter. It is the blockade of dopamine receptors in the limbic system, the reticular activating system and the forebrain which is the focus of the activity [5]. It has been suggested that the mode of action is not the suppression of dopaminergic overactivity but rather the combat or receptor supersensitivity in key dopaminergic synapses [3].

The minor tranquillisers differ from the major tranquillisers in that they are effective as anti-anxiety agents and also have positive effects in alleviating sleep problems. They are therefore widely used an anti-anxiety agents in clinical medicine for the treatment of a range of emotional and mental disorders within the general population. Families of drugs within this category include the benzodiazepines, the propanediols, beta-blockers and the barbiturates. Much of the clinical response to the minor tranquillisers is dose dependent. In small doses the minor tranquillisers exert their anxiolytic effect by allaying feelings of tension and anxiety. This is accompanied by a general feeling of fatigue and sleepiness. The barbiturates and the propanediols (including meprobamate) are powerful anxiolytic agents only in doses which produce severe drowsiness and an impairment in mental and physical performance. The benzodiazepine group of drugs act by facilitating the transmission of the inhibitory neurotransmitter gamma-amino-butyric acid (GABA) and therefore are more specific in their effect on the limbic system and produce anxiolytic effects in doses which do not have hypnotic effects. When administered in larger doses they become effective as hypnotics.

3. TRANQUILLISERS AS ANTI-ANXIETY AGENTS

At any point an individual's level of arousal, or level of CNS activation will be at some position along, *"a continuum ranging from comatose states or deep sleep to extreme excitement"* [6]. The exact position will depend on the physical and mental states of the individual. It has been suggested that *"when arousal levels are high an individual may experience unpleasant emotional and physical reactions associated with arousal of the autonomic nervous system"* [7] and that such reactions constitute stress or anxiety. It is these unpleasant emotional and physical reactions which are the symptoms of anxiety and stress and which anti-anxiety agents serve to reduce. The reduction of these symptoms is brought about by the chemical lowering of CNS activation in order to restore mood and anxiety levels. This occurs either as a result of direct lowering of the activity in the serotonergic and cholinergic nerve pathways of the CNS, or through reduced rates of noradrenaline production. One study reported that schizophrenic subjects, who suffer from an over-activation of the CNS, improved

their performance in a mental task of the ingestion of diazepam [5]. This was put down to the fact that activation levels were chemically lowered by the drug, thus restoring normal performance and reversing the negative effect of any initial over-activation.

The relationship between arousal and human performance has been well documented and there are numerous theories to explain the exact nature of the relationship [8]. Whether the relationship is linear, curvilinear, catastrophic or multidimensional is not of concern here. What is of interest is that for any individual an optimal level of arousal may be required to produce an optimal level of performance. Manipulation of arousal levels through behavioural or chemical means in order to achieve optimal levels are common practice in sport and exercise. The use of tranquillisers may be an effective tool which the over-aroused athlete can use to lower his arousal levels towards optimum.

Use of tranquillisers immediately prior to competition to combat the symptoms of pre-event nervousness could, in theory, be effective through lowering of arousal levels down to optimum. Whether this would work in practice is not certain. That arousal levels would be lowered is probably not in doubt. Careful selection of the dose and most appropriate drug in terms of half-life and plasma levels would enable manipulation of arousal levels to take place. Identifying and eliminating any possible adverse effects on physiological, psychological and performance factors would be more problematic.

Resting measurements taken after the ingestion of selected tranquillisers suggest that there may not be significant adverse effects on cardiovascular or respiratory parameters. No significant changes in selected cardiovascular parameters (blood pressure, pulse rate, stroke volume and cardiac output) or respiratory rates and volumes over an 8 h period after ingestion of triazolam (0.5 mg and 1.0 mg) or placebo have been reported [9]. Blood pressure in individuals after ingestion of 2.0 mg of alprazolam has been monitored and there was a decrease in both supine systolic and diastolic blood pressure 2 h after ingestion and no associated rise in heart rate [10]. In the same subjects after 5 min of standing there was an increase in both systolic pressure and in heart rate. A further study [11] reported that resting coronary blood flow was also increased with the ingestion of the minor tranquilliser diazepam whilst the major tranquilliser chlorpromazine increased heart rate but reduced blood pressure, stroke volume and peripheral resistance during exercise. Such observations do not suggest any obvious negative effects of tranquilliser ingestion on cardiac function.

Little literature exists concerning exercise performance immediately after the ingestion of tranquillisers. Observations on sub-maximal exercise have been made in a study in which subjects ingested a clinical dose (20 mg) of temazepam 30 min before prolonged sub-maximal exercise [12]. The duration of exercise achieved by the subjects was not significantly different from that achieved in a placebo trial. Heart rate, ratings of perceived exertion, plasma glucose and plasma lactate levels were not significantly different between trials, suggesting that temazepam had no significant effects on selected physiological or performance parameters. Weight loss and perceptions of thermoregulatory mechanisms during exercise were significantly different between trials with subjects reporting increased perceptions of heat and greater fluid loss in the temazepam trial. There is, therefore, a suggestion that the administration of temazepam prior to exercise may have an effect on thermoregulatory mechanisms.

Supramaximal exercise after the ingestion of tranquillisers may show a different response [1]. This study, in which subjects performed a Wingate power test 4 h after the ingestion of lorazepam (1 mg), resulted in a significantly lower peak power output during the test when

compared to a placebo trial. This was accompanied by a reduced maximum blood lactate level and reduced post-exercise adrenaline levels. The metabolic changes were reversed when subjects ingested caffeine, a CNS stimulant, alongside the benzodiazepine, but the power decrement remained.

The effects of a single dose on subsequent psychomotor performance have been better documented. Performance in simple discrimination and memory tasks is impaired, with an impairment in an auditory vigilance test after the ingestion of diazepam (5 mg) being observed [13]. This dose of diazepam also impaired the ability to select specific letters from pages of letters and decreased the short term retention of digit strings. The ability to learn information and then recall it again is also impaired with a dose-dependent response. Lorazepam (1 mg) impaired verbal learning by 11.5% and a 2.5 mg dose impaired performance by up to 30% [14]. The process of storing information may be affected rather than the process of retrieving learned information [15]. Diazepam is also shown to impair the ability to acquire information for later use and material learnt prior to ingestion of the drug can be recalled but information learnt after ingestion cannot be effectively recalled [5].

Performance in decision-making tasks such as reaction time and choice reaction time tasks are generally impaired by the benzodiazepines. Lorazepam (2.5 mg) significantly increased simple reaction time 4 h after administration in normal subjects [14] and simple reaction time was impaired by a mild tranquilliser; the greatest impairment occurred when subjects were uncertain as to when the stimulus would be presented [5]. Single doses of the benzodiazepines also impair performance in more complex cognitive processes. For example, alprazolam (2.0 mg) had significant adverse effects on a variety of cognitive tasks including tracking and word tests [10]. Acute (0.25 mg to 5 mg) doses of lorazepam [14], diazepam [16] and alprazolam [16] have all been shown to reduce the number of items correctly substituted in a digit symbol substitution test. It can be implied from the impairment in performance in this task that the minor tranquillisers impair the complex cognitive processes concerned with the encoding of stimuli [5]. Schizophrenic subjects showed an improvement in task performance after drug ingestion. A likely explanation is that the schizophrenic subjects are initially over-aroused and that the ingestion of the drug serves to lower arousal towards the required optimal for the task. Normal patients, however, are at optimal levels before administration of the drug but the drug serves to lower arousal below the optimum.

The nature and magnitude of any response are dose dependent and some studies report no adverse effects. Performance in a mental arithmetic task after ingestion of 5 mg of diazepam has been observed [13] and was found to be not significantly different from pre-drug performance. No adverse effects of temazepam (20 mg) on performance in a choice reaction time task or a mental addition task during exercise have been shown [12]. In this latter study, however, the authors suggested that the sedative effects of temazepam may have been overridden by the stimulus of exercise. The mechanism by which tranquillising drugs affect performance in cognitive tasks is uncertain. The pharmacological responses to such drugs include the blocking of the turnover or release of certain neurotransmitters including noradrenaline, dopamine and acetylcholine. This reduced activity in the neural pathways which may lead to the lowered performance as a result of lowered arousal levels.

For use of selected tranquillisers immediately prior to exercise performance to be accepted much more information is required concerning the exercise responses to particular drugs and in particular situations. In terms of CNS activation, arousal levels may be reduced by appropriate doses of selected drugs. This may be accompanied by no adverse effects on

cardiac function or metabolic function at rest [9] or during sub-maximal exercise [12] but decrements in peak power outputs during supramaximal exercise [1]. In addition, reaction times and cognitive processes may be adversely affected. Individuals wishing to lower arousal levels prior to sub-maximal exercise that does not pose excessive psychomotor demands may be able to do so successfully without too many adverse effects by taking selected tranquillisers in appropriate doses.

Athletes wishing to secure a comfortable night's sleep prior to competition may use tranquillisers to assist in this, although it has been suggested that healthy subjects with no sleep problems exhibit minimal improvement in sleep induction with hypnotic drug administration [17]. Observations of EEG do, however, suggest that athletes exhibit different sleep patterns than sedentary individuals [2]. Hypnotic agents may therefore be of use in aiding sleep in certain individuals. Temazepam (15 mg and 30 mg), and flurazepam (15 mg and 30 mg) have been shown to enhance selected sleep characteristics in healthy subjects [17]. Indeed, numerous studies clearly demonstrate that the benzodiazepines have a significant effect on sleep and wakefulness [18]. Of importance in the consideration of the effectiveness of benzodiazepines as hypnotics is the possibility of impairment of subsequent mental and physical performance.

The benzodiazepine family of drugs can be sub-divided into short-term and long-term according to their different half-lives. Single doses of the short-term benzodiazepines may well be cleared within 8 to 10 hours whilst effects of the long-term benzodiazepines may still be evident 12 to 36 hours later. The existence of an effect the morning after ingestion may lead to a residual impairment of performance. Such impairment of performance with overnight ingestion of selected tranquillisers may be an unwanted effect for athletes taking such drugs as a sleeping aid. The so-called "hangover" effect therefore needs to be considered when evaluating any drug and its subsequent effect on performance. Performance in a tracking task, a measure of visuo-motor coordination, was adversely affected up to 19 h after ingestion of flurazepam (30 mg) and nitrazepam (10 mg) [19]. There was no overnight "hangover" effect evident after diazepam (5 and 10 mg), temazepam (10, 20 and 30 mg) or oxazepam (15 and 30 mg). A 30 mg dose of temazepam impaired choice reaction time the morning after ingestion and the integrity of the central nervous system as measured by critical flicker fusion was also impaired the morning after ingestion [20]. Accuracy and reaction time in a rapid information-processing task has been reported to be impaired the morning after the administration of temazepam (40 mg) and flunitrazepam (30 mg) as a result of this "hangover" effect [21]. In contrast, no differences in choice reaction time or mental addition the morning after temazepam (20 mg) ingestion have also been reported [12]. In this case ingestion of the drug was followed by prolonged sub-maximal exercise and it may be that the stress of prolonged exercise overrides the depressant effect of temazepam and thus negates any "hangover" effect. It may not be only psychomotor performance which remains affected the morning after drug ingestion. Decrements in maximal isometric force the morning after administration of flunitrazepam (2 mg) have been reported [22] but no such decrement was evident after triazolam (0.25 mg) ingestion.

The general suggestion from the literature is that benzodiazepines with longer half-lives may still exert negative effects on psychomotor and physical performance (including maximal strength) the morning after their ingestion. The use of such drugs to improve sleep must therefore be carefully considered if an athlete is expected to compete, train or undergo physiotherapy as a part of a rehabilitation programme the morning after ingestion.

4. THE USE OF TRANQUILLISERS IN DESYNCHRONIZATION

With an increasing number of international competitions the occasions when athletes are expected to travel great distances are now the norm rather than the exception. International travel across time-zones can lead to the desynchronization of circadian rhythms and the general disorientation of jet-lag. The body usually requires time to readjust to shifts in its circadian rhythms but this resynchronization may be aided by behavioural and pharmacological means. Behavioural mechanisms to aid readjustment include alterations of social activity, meal times and sleep periods. Sleep is a strong synchronizer of circadian rhythms [2] and it is recommended that sleep be taken during the "new night time" rather than the "old night time". This may require individuals to attempt to sleep although they are not necessarily tired. Pharmacological mechanisms used to aid resynchronization include the hormone melatonin and the minor tranquillisers.

The minor tranquillisers may have a role to play in inducing sleep in those instances where individuals find difficulty in sleeping at the "new night time". Much of the research associated with circadian rhythms and benzodiazepine use has centred around shift workers rather than time-zone changes. Observations have suggested that selected drugs are effective in inducing day time sleep but less effective at keeping an individual asleep. One study [21] showed that temazepam assisted day-time sleep in shift workers without any prolonged impairment of information processing. It is possible that to be successful in resynchronization repeated doses of tranquillisers may be required over a period of several nights. Administration of repeated doses will produce different and exaggerated effects than single acute doses. Maintained plasma levels of the drugs and their metabolites may lead to exaggerated performance impairments and in extreme cases drug dependence. A further study [16] observed an increased reduction in performance in a range of mental tasks after one week continued administration of diazepam (5 mg/day).

The concern with the use of tranquillisers in resynchronization is the possible hangover effect and associated impaired performance. Athletes who travel for competition may experience physical and mental performance impairments with continued tranquilliser use and thus not be able to perform at optimum. If tranquillisers are to be used in resynchronization it is recommended that travel takes place well in advance of competition and that tranquilliser use be moderated to allow any negative performance effects to pass.

5. TRANQUILLISERS AS MUSCLE RELAXANTS

Therapeutically, selected tranquillisers demonstrate a muscle relaxant effect [3]. The benzodiazepines decrease voluntary muscle tone in normal individuals without affecting neuromuscular transmission [3]. They may be effective in reducing muscle spasms associated with pain. Such effects suggest a possible role for the drugs in the treatment of injured athletes. Concern over their use, however, exists given the fact that there may be a reduction in isometric strength the morning after ingestion of flunitrazepam [22].

Whether the reported muscle relaxant effects of tranquillisers are responsible for impaired motor performance and skill execution is uncertain. In general the administration of single doses of selected benzodiazepines on motor ability shows a dose dependent response. Increased amounts of the drug will produce a more profound effect. In most instances this

effect is an adverse one with performance being significantly impaired to varying degrees. For example, temazepam in 3 different single doses (10 mg, 20 mg and 30 mg) was administered to a group of normal healthy individuals and a dose-related response to performance in some elements of a battery of perceptual-motor tests was observed [23]. The tests which placed temporal and spatial demands on subjects were more sensitive to acute doses of temazepam than skills which placed less of a temporal and spatial demand. Smaller acute doses of diazepam (5 mg) and bromazepam (3 mg), however, did not produce any significant decrements in performance in a selection of motor skills in healthy female subjects [24]. The lack of difficulty of the tests used and the relatively low dose administered were offered by the authors as explanations for the study's failure to show any adverse effects of these two drugs.

The potential role of the tranquillisers as muscle relaxants in instances of spasticity and muscle spasm as a result of pain is not clear. Impaired muscle function may result from tranquilliser use and this may be reflected in diminished force output [22] or decreased motor ability [23].

6. SUMMARY

Tranquillising drugs do not appear on the International Olympic Committee's list of banned substances primarily because there is no evidence to suggest that they possess direct performance enhancing properties. On the contrary, there is much evidence suggesting that certain areas of human performance are impaired by ingestion of tranquillisers. The general observation is that the tranquillising drugs can impair psychomotor performance, motor ability, maximal isometric strength, and maximal power output both immediately after ingestion and up to 36 h afterwards. The degree of impairment is dependent on the drug form, dose and frequency of administration. Athletes suffering from anxiety, sleeplessness or desynchronization are advised to avoid the use of such drugs if they wish to compete or train at optimal levels within 36 hours of ingestion. Behavioural coping strategies may be more effective ways to relieve the anxieties of top level sport.

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Discussion: The Role of Tranquillisers in Sport and Exercise

K.A. Perkins:

There is a term in psychopharmacology called "state dependent performance", and the notion here is that if you are used to performing any sort of task in one drug state (usually drug absent) and you introduce a new drug state, that can impair performance, whether or not there is a true pharmacological action that impairs the performance, and sometimes it can even be the reverse. If you are used to performing in the presence of a drug and you remove the drug, because you have changed that drug state from drug present to drug absent, you can have an impairment in performance. That is another reason, (not so much for the anti-anxiety drugs, but many other psychoactive drugs), why it may be a problem to take new drugs prior to competition if you have not been performing under the influence of those drugs in the past, and this applies particularly to skill sports.

A. Miles:

Another problem is that a lot of the tasks that are used to measure performance here are subject to a learning effect as well, and you have to eradicate any learning effect within the task itself before you can actually identify any drug effect.

J.P. Clarys:

Could exercise play a role in the treatment of individuals dependent on tranquillisers?

A. Miles:

It has been suggested that one could use exercise as a means of taking away the dependence on drugs. The study that we performed actually showed that the effects of temazepam were overridden by the stress of exercise.

J.P. Clarys:

We have studied the influence of different doses of triazolam, diazepam and flunitrazepam, on different levels of strength and velocity. At one point in that study, we combined them with alcohol and we felt that there was more need for studying combined situations. What is your opinion about the effect of drug combinations?

A. Miles:

The important thing here is that you have to decide whether or not the positive effects of the benzodiazepines are going to be of potential use, and then perhaps look at mechanisms which can actually stop the negative effects. Theoretically, caffeine could have a potential role to play there in conjunction with the benzodiazepines. As a stimulant, it might actually reverse some of the negative psychomotor effects. However in one study, in which caffeine was used in conjunction with benzodiazepines it was found that the changes in lactate and in adrenaline were actually ameliorated with the presence of caffeine, but there was no actual effect on the power output. So the performance was still impaired, but the metabolic changes were reversed.

J.P. Clarys:

While we were doing that type of studies we were surprised to see that there were different lists of doping depending on the country, and that they were often different from the Olympic doping lists. On some of those lists we found benzodiazepines and on others we did not see them. Is there an explanation?

D.A. Cowan:

The International Modern Pentathlon Federation for example bans benzodiazepines. They also ban major tranquillisers and as an olympic sport, participate in the Olympic Games. The actual logic behind just what is banned and what is not is sometimes rather difficult to deduce, and I think we just have to accept that sometimes there is not much logic in what is banned and what is not.

F. Brouns:

What are the effects of tranquillisers on events like shooting, where high precision is required?

A. Miles:

There is evidence to suggest that motor skills are actually impaired, but there is a possible role for them within their muscle relaxant context, in aiming sports and precision. This is the reason why the modern pentathletes have them as a banned substance.

D.A. Cowan:

Some take the view that benzodiazepines do not help pistol shooters very much, because they are so laid back they could not care where the target is.

T. Reilly:

One aspect that one should consider is that in many studies where alcohol does not show an effect, nor do any of the benzodiazepines show an effect, the additive influence comes through quite clearly. There may be a very strong effect when the two are used in combination.

P.M. Clarkson:

Are there studies looking at the effects of benzodiazepines on the types of sleep?

A. Miles:

Yes, there have been studies related to the quality of sleep and the type of sleep. Some of the studies have suggested that normal healthy individuals who are subject to normal sleep patterns are not adversely or in any way affected by benzodiazepines. Problems seem to be associated with people who do demonstrate irregular sleep.