"An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage", is how pain is defined by the International Association for the Study of Pain (IASP) (1). Chronic pain is a sub- classification within this specifically referring to pain persisting or recurring for more than 3 months (1).

Pain is an extremely complex concept and the models used attempting to accurately visualise its effects have evolved over the course of history. Currently the most popular model of pain used worldwide is the biopsychosocial model, popularised by the work of George Engel in the late 20th century (2). This proposal challenged the previously accepted pathoanatomical model of pain- which describes symptoms to be based on the presence of specific structural pathology (2). In contrast to this, the biopsychosocial "is a broad view that attributes disease causation or disease outcome to the intricate, variable interaction of biological factors, psychological factors and social factors" (2).

Chronic pain is estimated to affect between one-third and one-half of the UK population, equalling close to 28 million adults (3). Complications of chronic pain, if not properly treated, include significant disability, psychological distress (including depression and anxiety), medicine misuse and an overall reduction in quality of life (4). The massive prevalence and devastating consequences of chronic pain, if not treated properly, clearly justify the prioritisation of optimising its management.

Figure A (5):

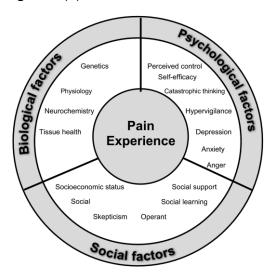


Figure A lists some examples of sub-classifications within each of the 3 areas of the biopsychosocial model. The figure also illustrates how pain, experienced by the patient, is at the interplay of all of these different factors.

There was initially some resistance to the acceptance of this model of pain by some clinicians, as the concept of complex interactions between 3 major domains makes it an impossible task to isolate the pain as a separate entity from the patient themselves (2). This makes an approach to optimal treatment considerably more difficult and limits the potential efficacy of certain interventions, including manual therapies, in comparison with the pathoanatomical model where structural pathology was thought to be solely causative of

symptoms (2). For clinicians at the time, having dedicated their careers to specialising in performing these therapies, the idea that pain had many more diffuse components, was understandably difficult to accept (2).

Despite this, under the biopsychosocial model of pain, the efficacy of management strategies is not necessarily restricted. Instead, it is required that the form these interventions take must evolve, congruent with our developing understanding of the contributing factors to pain. This is especially true in the context of chronic pain and functional diseases, where all measurable biological processes are seemingly normal, and the psychological and social elements may be the most considerable contributors to symptoms.

This modern attitude towards pain management is already reflected in the National Institute for Health and Care Excellence (NICE) guidelines regarding chronic pain, revised in April 2021, which lists treatment options as: exercise programmes and physical activity, psychological therapy, acupuncture and pharmacological therapy (4). Across these management options, all 3 areas of the biopsychosocial pain model can be targeted as appropriate. The purpose of this essay is to explore how existing exercise programmes and physical activity can be improved for utilisation in chronic pain management within the NHS.

Exercise is well documented in existing literature to improve chronic pain- the mechanism by which the full extent of these benefits are elicited is incompletely understood, however it is known to be complex and multi-factorial (5). Some proposed mechanisms include the systemic anti-inflammatory effects of exercise, by cytokine mediation, which prevents or reverses hyperalgesia (5). In addition to this physical activity triggers the release of endogenous opioids, producing an "exercise-induced analgesia" (EIA) which reduces the perception of pain both during and after exercise (5). Another mechanism explores the role of the neuroendocrine system, as exercise is known to trigger a stress response- affecting the levels of neurotransmitters including serotonin, dopamine and noradrenaline (6). This plays a role in correcting the imbalance of these chemicals present in chronic pain patients (6). Exercise has also shown the ability to reverse the molecular and cellular changes in the spinal cord and brain found in patients suffering from chronic pain (7). An example of this reversal process is axonal nerve regeneration, which better the central nervous system's ability to responds more proportionally to pain signals (7).

The Public Health Advisory Committee (PHAC) produced NICE guidelines on exercise referral schemes in 2014 which judged the commissioning, development, and delivery of current exercise referral schemes to not meet the standard threshold for a cost-effective health intervention, based on pound per quality-adjusted life year gained (8). Economic analysis found existing schemes are less cost effective than giving brief advice regarding exercise in primary care, as the schemes are more expensive in comparison and found to produce little additional effect to the exercise level in individuals (8). However, it was also deemed there was considerable uncertainty regarding the correct parameters to use for economic modelling purposes and that not all of the potential benefits were captured (8). Due to this the PHAC decided there not to be sufficient evidence to recommend disinvestment into these schemes (8).

The first line recommended pharmacological management for chronic primary pain in adults is an antidepressant including selective serotonin reuptake inhibitors (SSRI) (4). SSRI drugs pose a risk for a multitude of side-effects including gastrointestinal symptoms, gastrointestinal bleeding, hyponatraemia, anxiety and agitation (9). Citalopram is one of the drugs recommended which has an additional risk of QT interval prolongation and torsade's de pointes, a dangerous cardia arrythmia, secondary to this (9). While SSRIs do not meet the definition of a truly physiologically addictive substance, there are also risks of discontinuation symptoms including mood change, restlessness, sleeping difficulty sweating and paraesthesia (9). In addition to this, despite not featuring in current NICE guidelines, it is estimated 25-30% of chronic pain patients are currently taking opioids (4). These medications are dependence forming, therefore in addition to a non-desirable side-effect profile, these patients also develop tolerance and doses become ineffective at controlling symptoms if not escalated accordingly (4). The risk of harm from opioids is known to increase significantly at doses exceeding the equivalent of 120mg/day of oral morphine, with no increased benefit (4).

Considering the non-exhaustive list of drawbacks highlighted above, it is clearly in the best interests of patients for pharmaceutical managements to be avoided if possible. While their complete elimination among the chronic pain population is obviously unrealistic, exercise therapies do have the genuine potential to effectively manage a significant proportion of patients, secondarily avoiding escalation to medical treatments. Findings of the PHAC review, however, demonstrate the existing structure of exercise regimes to be inefficient and requiring improvement for the full extent of benefits to be experienced.

Current existing exercise programmes within the NHS take a wide variety of forms. This includes both supervised and self-directed formats, aerobic and resistance training style sessions, commissioned leisure centre memberships (gymnasium, swimming) and outdoor activity classes (running, cycling etc).

The PHAC review noticed there was variation cost effectiveness depending on format - with the logical findings that self-directed and less resource reliant activities were cheaper to maintain (8). They found an important factor for increasing the effectiveness of an exercise programme to be improving adherence throughout the schemes duration and after the scheme had finished (8). An interesting figure highlighting the severity of lack of compliance is that it takes 36 patients to be referred for just 1 to perform exercise at the recommended levels (8). This statistic demonstrates improving compliance is the most pertinent factor, above all others, that should be prioritised to increase the efficacy and cost-effectiveness of exercise programmes. While differing training styles, aerobic in comparison to resistance training for example, may vary in the extent of benefits for chronic pain patients- these differences are negligible if, as statistics suggest, 35 out of 36 patients being referred failing to engage with them appropriately. Therefore, in concordance with this relative weighted importance, the remainder of this essay looks to assess in detail some of the theory into how improved compliance can be achieved.

Approaching this problem from the perspective of an evolutionary biologist can give fresh insight into some of the fundamental concepts of how to make exercise more achievable for

chronic pain patients. This essay views chronic pain patients as human beings- governed by powerful evolutionary tendencies, which if better understood, can hopefully be used to manipulate exercise into a form that is the most natural and enjoyable. Daniel Lieberman is a professor in the Department of Human Evolutionary Biology at Harvard University and is a leading figure in the world of human evolution, renowned for his research related to exercise and its relevance to health (10). His book 'Exercised', some of the content from which will be discussed below, assesses the science of physical activity, rest and health from the perspective of an evolutionary biologist (10).

Lieberman defines exercise as 'voluntary physical activity that is planned, structured, repetitive and undertaken to sustain or improve health and fitness' (10). The word voluntary in this definition insinuates that exercise is physical activity that is not strictly necessary. Findings of an anthropological study conducted on the Hazda, a primitive hunter-gatherer tribe in Tanzania where humans evolved from, suggest there is a natural tendency to move as little as possible (11). Despite living in extremely harsh conditions, adults were found to perform an average of three hours forty minutes performing light activities (for example collecting berries, often in groups while chatting) and only 14 minutes of moderate or vigorous activity (11). Despite being significantly more than the average level of physical activity performed by individuals in the UK, these durations are far from being an extortionate volume of physical activity- reiterating that humans have not evolved to perform physical activity where it is not necessary (10). In the UK modern-day society this provides novel problems, where the abundance of technologies commonly available provide extreme convenience and the ability to survive comfortably while performing minimal physical exertion. Taking the evolutionary traits and modern environmental factors in combination, it is very understandable why many of the population choose to lead sedentary lifestyles and why problems with exercise scheme compliance have been encountered.

From the perspective of an exercise scheme provider, it would be tempting to view a lack of compliance as a problem the patient is to blame for, as they are failing to take ownership of their health and engage properly with the programme. While this may be partially true, ownership of the problem should instead be adopted by the exercise provider, for improvements to be made. The lack of compliance currently present highlights a fundamental lacking in the structure of the exercise schemes, making them unengaging and difficult to adhere to- which if addressed correctly can be improved.

Despite the large percentage of people failing to meet the recommended levels of exercise, there is paradoxically also a widespread narrative that people ought to be exercising more and that it is detrimental to not perform enough of it. This attitude has been commonly held since the 20th century, fuelled by a variety of factors. One contributor has been nationalist government campaigns promoting physical strength amongst its population, through fear of a lack of fitness amongst its soldiers (12). Another is through health anxiety, communicated from politicians and educators, who fear the health consequences of a growing lifestyle of physical inactivity (12). This would suggest it is not through any lack of awareness of the benefits that the population, including the chronic patients whom this essay concerns, do

not exercise enough. This information is useful because it suggests despite the knowledge that performing physical activity is desirable, many still find motivation towards prioritising consistent forms of exercise difficult.

Lieberman approaches the topic of promoting exercise effectively by either making it necessary or fun (10). This is a somewhat difficult task because an integral part of the definition of exercise is that it is voluntary, and therefore unnecessary, physical activity. In addition to this, amongst the plethora of technology in modern society, specifically in the entertainment and leisure sector, there are many distractions to compete with. Therefore it is more difficult for a physical activity to appear a fun and appealing way of spending time.

Despite these challenges there are still some measures that can be taken. The aspect of making exercise fun revolves largely around making it a social affair. Humans are a deeply gregarious species and historically organic forms of physical activity take the form of gathering food which is performed in groups, as observed in the Hazda tribe mentioned previously (10). The socialising surrounding exercise provides opportunity for collaboration and praise which both act as deterrents to quitting. Other factors to make exercise more fun include playing sports or games (10). 'Play' is defined as an activity with no serious practical purpose- performed by all young mammals to acquire social and physical skills (10). Humans are one of the few species to also play as adults, and they are unique to do this in the context of sports, which is a distinctive human behaviour common to all cultures throughout history (10). The universal prevalence of sports in cultures is an interesting observation because it demonstrates this to be a very good example of where humans have performed physical activity naturally, even when it provides no benefit, purely for enjoyment.

The alternative to incentivising exercise participation by making it fun is to make it a necessity. The CEO of the Björn Borg sportwear company in Stockholm provides a real-world example this concept, where attendance of a collaborative 'Sports Hour' session is mandatory every week for all his employees (10). Other, less authoritarian, methods by which a person's daily routine can be changed to account to this, include scheduling a session with a friend or social group. The pre-planned nature provides some social obligation and accountability for the individual to attend. Other examples include manipulation of the household or work environment to make physical exertion more convenient than the alternative, for example taking the stairs instead of an escalator (10).

The most significant common aspect to both strategies by Lieberman was introducing a social element to exercise. As highlighted previously, this simultaneously makes the process of 'unnecessary' physical activity more enjoyable while the social obligation of a planned group session gives attendance and proper completion the illusion of being a necessity. This social component should therefore be heavily prioritised when designing the structure of exercise referral schemes for chronic pain patients.

A logical form for these schemes to take would be as team game activities, congruent with their constant prevalence throughout history. This would maximise the level of social interaction and cooperation within a group session, demanded as an integral aspect of the exercise. In practical terms, taking cost-effectiveness into account, this would be most

achievable by running outdoor sports which therefore have a smaller cost of organisation. A pre-empted potential drawback of this setup would be the requirement of a critical number of attendees for any games to be able to run. One possible solution to this would be only initially offering a small number of sport options, therefore allowing classes to fill more quickly. The obvious choices would be outdoor sports which are most popularly participated amongst the target population, which may vary across the UK, depending on the prevailing socioeconomic status and ethnicity for example. If future studies found a corresponding increase in compliance, as would be hoped for, this would merit an increase in public investment and open the possibility of introducing other more diverse sports which are more expensive to run. Using football as an example, a sports hall could therefore be used as opposed to outdoor fields, encouraging engagement throughout winter months of the year.

An alternative to a game format, while maintaining a strong social element, would be preplanned group walks or open-water swimming sessions (if the location and climate allows). These style formats may be preferred by some patients, however emphasis would have to be placed on the social element to the session, where the group would commence at a specific pre-planned time and location.

In summary, this essay outlined the currently accepted biopsychosocial element of pain and the corresponding treatment options existing in NICE guidelines for chronic pain. It was shown a significant proportion of patients receive pharmacological from dependent forming medications which should therefore be avoided where possible, and exercise therapies to have the potential of achieving this. When assessing the current forms of exercise therapies for strengths and weaknesses it was quickly obvious a lack of patient compliance was the dominating limiting factor, which at this stage should be solely targeted for making improvements. The main finding of how to go about this was by emphasis of the social aspect of exercise- in practical terms these should take the form of either game-based sports or pre-planned outdoor activities. While these suggested improvements may only seem simple and logical, their explanation through principles of evolutionary biology have hopefully justified why these are in fact the types of structural changes with the largest potential to pursue.

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