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RESEARCH ARTICLE



# Retrospective review of the efficacy for sublingual ketamine in the treatment of chronic low back pain defined by a cause and central functional pain symptom focused clinical model

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**ABSTRACT**

**Purpose:** Chronic low back pain is a leading cause of disability worldwide. A clinical model for its cause is lacking. Defining a cause based clinical model and a framework of understanding back pain in terms of peripheral structural and central functional pain is essential for optimal management.

**Materials and methods:** We describe the results of the largest published audit of 41 chronic low back pain patients, receiving outpatient sublingual ketamine therapy for defined central functional pain along with conventional peripheral structural pain management. Our clinical model assigns Movement Dysfunction as the primary cause for low back pain symptoms and restores it with Movement Therapy focused rehabilitation which is also defined. Patients were derived from a tertiary single neurosurgical specialist practice in Brisbane Australia over a three year period.

**Results:** Severe pain and disability measurements more than halved and only 13% of patients ceased ketamine prematurely due to predominantly non-sinister side effects common to all pharmaceutical therapies. All other surveyed metrics of utility were highly favourable in this challenging cohort of chronic back pain patients biased to poor outcomes.

**Conclusions:** Outpatient ketamine maintains high efficacy and safety used in conjunction with a unique clinical model that describes chronic low back pain.

**IMPLICATIONS FOR REHABILITATION**

- This paper builds on our previous publications that describe the disease of movement dysfunction as an integral factor to the development of a cause based clinical model for the condition of chronic low back pain symptoms.
- Our clinical application of this model, applying the necessary dual approach of controlling symptoms arising from peripheral structural pain and central functional pain in conjunction with elimination of root causation has shown favourable outcomes in patients with high levels of pain and disability based on their tertiary referral origin and high Oswestry Disability Scores.
- Removing chronic low back pain from its position as one of the world's leading causes of pain and disability is more likely if the rehabilitation industry can replicate and test treatment algorithms based around established clinical models of disease which is the important subject of this paper.

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## Introduction

Back pain is recognised in Australia and equally significantly in the industrialised world as the second leading cause of total disease burden and disability adjusted life years. It sits slightly behind cancer and coronary heart disease, both similarly problematic in our society. More startling is that over the last two decades the impact of chronic low back pain has worsened while that of other highly burdensome conditions has improved. The industry wide failure to improve on the alarming and economically significant increasing prevalence of chronic low back pain cannot be attributed to the association of an ageing population [1].

A clear model for the cause of back pain is necessary to better assess and manage pain which is defined by the International Association for the study of Pain (IASP) as "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" [2].

Pain in and of itself is a symptom not a primary cause. The term "back pain" should not be used interchangeably as both symptom and diagnosis, although this misunderstanding is frequently observed [3]. Universally sound and successful medical intervention is dependent on addressing both symptoms in conjunction with eliminating cause [4].

We describe a clinical model and pain categorisation framework that guides the optimal cause-based management of pain, dividing it into two groups. Firstly, the well understood "Peripheral Structural Pain" and secondly the more nebulous "Central Functional Pain," conventionally and ambiguously referred to as Central Sensitisation.

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Contained within the domain of Peripheral Structural Pain are:

- Inflammatory pain
- Nociceptive pain
- Neuropathic pain

All of which are described by defined physiological mechanisms permitting effective diagnosis and symptomatic treatment [5,6].

Note that using this framework, neuropathic pain is distinct and not grouped with central functional pain or central sensitisation. Previously numerous authors have grouped central sensitisation as a form of neuropathic pain, chronic regional pain syndrome or reflex sympathetic dystrophy. Using this simple and more rational framework of understanding, neuropathic pain is distinct and not grouped with central functional pain or central sensitisation even though it is nerve mediated. Neuropathic pain arises when a definable neural structural injury exists causing neuropathic pain symptoms anatomically appropriate and specific to the injured nerve [5,7].

Central functional pain is poorly described by clinicians and even more poorly understood by patients suffering from it [8]. Brazenor et al. allude to this in their review of 751 central sensitisation publications, concluding that they found no convincing evidence that central sensitisation can persist as an autonomous pain generator in the human after resolution of the initial painful injury. They identify a multitude of psychosocial confounding factors in the diagnosis and conception of central sensitisation using currently held gold standards of Quantitative Sensory Testing and the Central Sensitisation Inventory of Nijs and co-workers [9–11] (Figure 1).

Our preferred pain framework dismisses with the concept that central sensitisation behaves as an autonomous pain generator. Brazenor et al. described a "dearth of evidence" for the autonomous pain generator driving Central Sensitisation [8]. The "dearth" likely relates more to inadequate and inconsistent definitions of centrally sensitised low back pain and the absence of a robust, reproducible, and testable clinical model for the condition of back pain rather than a lack of evidence per se. Referencing central sensitisation in terms of an Autonomous Pain Generator frames it in the light of a structural entity which may be misleading given that structural pathology does not exist for truly functional disorders. The term Central Functional Pain is therefore preferred to improve understanding and treatment.

Severe pain and disability with hallmarks of allodynia and hyperalgesia characterise central functional pain [8]. We view this as a secondary neurological functional disorder manifesting as pain. This concept is equivalent to accepted models of functional diseases such as depression or schizophrenia. They represent a functional (neurological) disorder manifesting with psychiatric symptoms [12,13]. Likewise central functional pain represents a neurological disorder manifesting with pain symptoms [14]. Neither possess a visible structural lesion to account for the condition and are therefore representative of a functional disorder. The previously described psychosocial factors that were felt to confound the diagnosis of central sensitisation likely represent predisposing associations that may incline an individual to be more susceptible to developing the central functional pain disorder after the triggering primary structural painful injury to the lumbar spine [15,16]. The diagnosis of central functional pain is reached when pain and disability present, out of keeping with the degree of structural compromise to the lumbar spine and para spinal soft tissue. We assert that central functional pain and peripheral structural pain are not mutually exclusive and often coexist [6,17]. This is of great importance for successful back pain management.

Our clinical model stipulates that a functional neurological disorder is driving central sensitisation and mandates an appropriate neurological remedy. Logically for success, the intervention must address the root cause neurological disease in conjunction with controlling the neurological central functional pain symptoms.

We regard isolated symptom-based management of back pain to be futile. This is consistent with central tenets of sound medical practice – eliminate causation in conjunction with controlling symptoms [4]. Neglecting this fundamental principle is likely to result in recurrence, chronicity and progression of symptoms. Reflecting the current reality of chronic back pain in our society.

Our clinical model postulates the existence of a primary disease, Movement Dysfunction, active in an acute or chronic form, by way of a sudden strain injury or accumulative subclinical poor spino-pelvic bending biomechanics respectively which causes biomechanical stress which drives biological inflammatory and/or nociceptive pain (peripheral structural pain) and ultimately premature motion segment structural compromise. Movement dysfunction is observable as a poor expression of default hip centric rotation, neutral spine maintenance and posterior kinetic chain powered movement for tasks of daily living be they trivial or physically demanding [18–20]. Movement Dysfunction left chronically unresolved and driving further peripheral structural pain is felt to cause and hinder the resolution of secondary central functional pain [21,22]. Pain symptoms clearly corrupt movement and the vicious cycle of corrupted movement driving more pain necessarily requires interruption [23]. The importance of specific Movement Therapy, distinct from conventional rehabilitation methods with a preponderance for stretching, core-strengthening, fitness and manual therapy, all of which have zero to only a coincidental effect on movement proficiency cannot be overstated in the application of this clinical model [23–27].

We describe clinical outcomes from long-term use of sublingual Ketamine to address the neurological central functional pain symptoms in conjunction with functional movement therapy to address the primary lumbar spine peripheral structural pain generators for chronic low back pain.

The NMDA (N-methyl D-aspartate) ion channel receptor found at most excitatory synapses belongs to the family of glutamate receptors responding to the neurotransmitter glutamate [28].

The clinical utility of ketamine in chronic pain states is felt to arise from its mechanism of action as an NMDA receptor antagonist. At sub-anaesthetic doses ketamine is recognised to have analgesic actions controlling pain that is not sensitive to other first or second line agents including anti inflammatories and opioids. Pain qualities characteristic of central pain including hyperalgesia and allodynia maybe more responsive to ketamine as opposed to conventional analgesics [29].

Ketamine may possess other benefits through opioid sparing and mechanisms acting on gene expression and signalling cascades that continue to act long after the drug has been eliminated as well as by promoting NMDA receptor hypofunction that is associated with reduction in memory and theoretically the memory of pain which would by definition be a neurological construct [30,31].

Parenteral routes avoid first pass metabolism but are problematic because of the narrow therapeutic window and expense associated with preparation and administration. Given the expanding clinical application and prevalence of chronic pain, a greater understanding and experience with transmucosal and oral routes for chronic use is of significant value [32].

**Peripheral Structural versus Central Functional Pain Framework**

| Peripheral Structural Pain | Central Functional Pain |
|---|---|
| **Nociceptive Pain**<br>Activation of discreet pain receptors within tissue<br>E.g.<br>Pulling hair, feeling something sharp or hot, a grit of sand on your cornea | **Central Nervous System Mediated Pain (Central Sensitisation)**<br>Functional pain not requiring persistence of peripheral structural pain generators. Able to amplify and modify afferent peripheral structural pain stimuli. Perpetuated by the persistence of peripheral structural pain afferent stimuli.<br>E.g.<br>1. Low back pain that was initially episodic but transforms into chronic low back pain in the absence of recognisable persistent structural injury.<br>2. A recognised traumatic lumbar strain injury that has a clear temporal and mechanistic relationship with the onset of peripheral structural pain but fails to resolve synchronously with healing of the primary structural pain generator.<br>3. Phantom pain – the presence of persisting (phantom) limb pain not attributable to neuropathic stump or other peripheral structural pain generators previously contained with-in the amputated extremity.<br>4. Whiplash associated disorder persisting months to years after the inciting "whiplash" event.<br>5. Post discectomy persistent back pain arising after surgery for lumbar disc prolapse after confirmation of healing and stability of the primary and surgical disc injury and long after the sciatic pain resolves.<br>6. "Failed" Back Pain Surgery Syndrome (stabilisation – fusion or disc arthroplasty) – successful and uncomplicated lumbar stabilisation that fails to reverse the primary presenting back pain symptoms. |
| **Inflammatory Pain**<br>Activation of the cascade of numerous acute inflammatory mediators that cause direct and indirect pain (e.g. swelling)<br>E.g.<br>"Sunburn" evolving after a day at the beach, sinusitis, bursitis, dermatitis or a blister, arthritis (joint related pain of chondritis, capsulitis, osteitis), tendonitis, myositis | |
| **Neuropathic Pain**<br>Painful activation of a discreet sensory nerve conveying a noxious stimulus<br>E.g.<br>Trauma to the ulnar nerve at the elbow (knocking your funny bone), a disc prolapse compressing a lumbar nerve causing "sciatic" pain | |

**Pain subclassifications described above are not mutually exclusive and often coexist**

**Figure 1.** Peripheral structural versus central functional pain framework.

Our formulation consisted of 50 mg ketamine lozenges each scored in quarters enabling easy division into four × 12.5 milligram cubes. Each dispensed tray consisted of 30 lozenges equating to 120 doses of 12.5 mg cubes.

Chong et al. describe this lozenge formulation to be stable for 14 weeks, practical for storage at room temperature (approximately 25 degrees Celsius) or in refrigeration [32]. Oral and sublingual bioavailability of ketamine and its active metabolite norketamine is comparable to intravenous ketamine at doses of 25 mg oral/sublingual and 10 mg intravenous, respectively. The median half-life for intravenous oral and sublingual administration are similar at 5.2 h. Other studies have shown shorter half- lives ranging from 2 to 3 h. 8 h post dosing comprises 2–2.5 half-lives and is felt to be the time frame for appreciable physiological effect.

Other troche ingredients include PEG 32, acacia senegal gum, silica, purified stevia extract and sodium saccharin.

Currently there are no treatment paradigms that provide long term consistent structured symptom and caused based treatment of central sensitisation conceptualised as secondary central functional pain in conjunction with consolidated reversal of the primary spinal peripheral structural pain generators.

## Methods

After conducting advanced PubMed search terms of Ketamine, sublingual and back pain we conclude confidently that our research represents the largest clinical audit of outcomes for patients with chronic low back pain, receiving outpatient sublingual ketamine therapy. Patients were derived from a single neurosurgical specialist practice in Brisbane Australia over a three year (October 2018 and November 2021).

Adopting a cause and symptom focused approach to curing chronic low back pain, the following paradigm was applied for the selection of patients and delivery of management consisting of sublingual ketamine in conjunction with Functional Movement Therapy (Figure 2).

Clinical assessment of peripheral structural pain centred around history, examination and magnetic resonance imaging of the Lumbar spine/sacroiliac joint. Clinical features of mechanical pain, discogenic pain or neural compression correlating with radiological

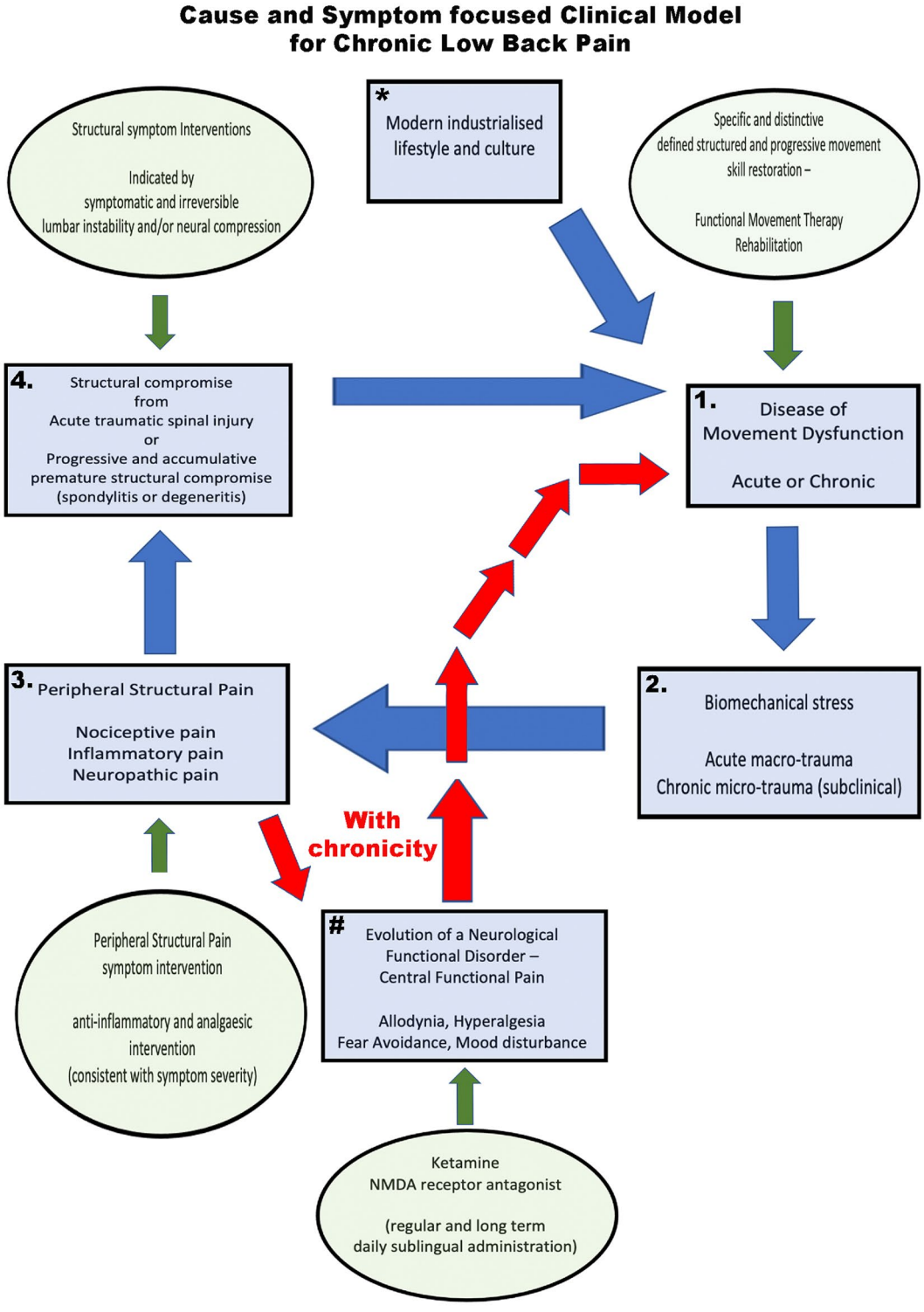


**Figure 2.** Cause and symptom focused clinical model for chronic low back pain.

imaging were addressed with the most appropriate and least invasive symptom focused remedy.

Clinical assessment of central functional pain centred around the same history, examination and MRI imaging. Central functional pain was deemed to be a significant contributor to the overall presentation if pain and disability remained high in the absence of clear peripheral structural pain generators or despite adequate treatment of recognised peripheral structural pain generators.

For example, if a patient had previously had an uncomplicated lumbar fusion for spinal instability but continued to suffer severe low back pain symptoms, they were deemed to be candidates for ketamine to address central functional pain. Another non operative and common example of ketamine utilisation for central functional pain is in the injured worker after a minor nonspecific strain injury to the lumbar spine occurs with persistence of symptoms into chronicity despite relatively minor structural compromise evident on MRI imaging. Typical findings of facet joint effusion or disc annular high intensity zones may validate the initial injury which stimulates nociceptive and inflammatory peripheral structural pain. Facet arthritis and annular tear respectively is appropriate terminology in that time context. If pain and disability persist well beyond the expected time frame for these relatively minor structural injuries to fully heal the primary driver for pain in this instance can be considered as central and functional in origin with the MRI structural findings in this context and time, more appropriately referred to as non-pain generating facet arthrosis and annular high intensity, respectively. More broadly speaking, spondylosis and degenerative change, all be it premature, are common and appropriate descriptions in this chronic setting, as the dominating driver of pain and disability is more likely central and functional in origin in contrast to peripheral and structural. Importantly, appreciating that the evolution of the central functional pain is a secondary consequence of the primary peripheral structural pain.

Persistence of severe pain and disability well into chronicity despite optimal first line management with appropriate rest, analgesics/anti-inflammatory and graded physical rehabilitation justified the diagnosis of secondary central functional pain and treatment with ketamine. The secondary development of central functional pain also emphasises the importance of early and optimal treatment of peripheral structural pain arising from even minor lumbar strain injuries.

Functional movement therapy was a mandatory addition to ketamine utilisation. Movement therapy consisted of two sessions per week over a period of eight weeks. Each lesson was delivered in a group setting at one location and conducted by at least two Movement Therapist's. The sole objective of the Movement Therapy was to reinstate a default motor pattern for the functional tasks of daily living, requiring the expression of hip centric rotation, neutral spine maintenance and posterior kinetic chain powered movement [19].

Data was collected by one medical student and one medical reception staff who were provided with an objectively structured, replicable questionnaire exploring outcomes and perception of ketamine use in our patients with chronic low back central functional pain symptoms.

Responses to these questions provided insight into the efficacy of outpatient sublingual ketamine utilisation for central functional low back pain. The survey questions explored:

1. History of back pain duration
2. Effect of ketamine on back pain
3. Duration of ketamine use
4. Pain medication use prior to commencing ketamine
5. Numerical pain scores pre and post ketamine use
6. Perceived percentage of pain relief with ketamine use
7. Perceived qualitative improvement with ketamine use
8. Perception of ketamine working differently to other pain medication
9. Ketamine side effect related questions
10. Concurrent participation in functional movement proficiency focused rehabilitation
11. Utility of ketamine for persisting back pain post lumbar spine surgery
12. Patients' advocacy of ketamine to a friend or family experiencing similar symptoms

Ketamine was dispensed from a single pharmacy in take home trays consisting of $30 \times 50$ mg troches. The starting dose was 12.5 mg (1/4 of one troche) sublingual nocte 15 min before bedtime. Over time gradual dosage escalation was permitted. Dosage escalation required consultation with the treating neurosurgeon to confirm the absence of side effects, adherence to Functional Movement Therapy and in particular exclusion of the development of concomitant peripheral structural pain generators. 12.5 mg BD up to a maximum dose of 12.5–25mg TDS was the dosing regimen range and dependent on symptom response and side effect profile.

## Results

Between October 2018 and November 2021, 108 patients were prescribed ketamine for low back pain comprising central functional pain elements. An additional 26 patients with central functional neck pain were also prescribed ketamine. Neck pain patients were not included in this audit. Our data represents the largest published series to date for outpatient ketamine use for chronic central functional low back pain.

Of the 108 potential patients retrieved from our database. 41 patients were able to be contacted. All 41 were happy to conduct the telephone interview. The remaining 67 patients were not interviewed because they were uncontactable via our telephone records. Due to time constraints and personnel, repeated attempts to contact these 67 patients was not possible. The 41 patients that were contacted are felt to represent an adequately large and representative random unbiased selection of the total 108 patients.

### *Back pain duration*

The average duration was six years and ranged from 2 to 20 years. One patient described lifelong low back pain.

### *Questions relating to impact of back pain on function*

Responses revealed that all patients were impacted in the range of 7–8 out of 10 in regard to sleep disturbance, ability to perform simple activities of daily living, mood, social activities, work/job requirements.

### *Questions relating to prior or concurrent pain medication use*

90% of patients had received prescription pain medication. 68% had trialed opioids and 24% had tried at least two different forms of opioid based analgesics. 50% regularly self-medicated with

over-the-counter anti-inflammatories and acetaminophen. One patient had trailed medicinal cannabis and one patient had trailed Orphenadrine.

#### *Duration of ketamine use*

Average utilisation was four months (equating to two prescriptions) and ranged from 3 to 24 months. One patient utilised ketamine for two years and ultimately was cured of his 10 year history of chronic low back pain. The same patient restored functional capacity consistent with amateur high-level athleticism.

#### *Questions relating to symptomatic improvement*

Prior to ketamine the numerical pain scale (0–10) average score was 8 and ranged from 4 to 10. After ketamine utilisation the average pain score was 4 and ranged from 0 to 10. Describing pain relief in terms of percentage improvement ranged from 0 to 100% improvement with an average improvement of 35%.

Greater than 50% of patients had at least 50% reduction in numerical pain score. Overall, 30% of patients recorded greater than 50% reduction in pain score. This is consistent with a significant majority of patients, 80%, describing a qualitative perception of improvement of greater than 80%.

#### *Questions distinguishing ketamine from other pain medication*

52% of patients felt that ketamine provided relief different to other pain medication and 73% would recommend ketamine to friends or family if they were experiencing similar pain symptoms.

#### *Questions relating to prior spinal surgery*

24% had prior spinal surgery and persisting low back pain after surgery. All of these patients reported further benefit in the questions relating to symptomatic improvement. All of these patients would recommend ketamine to friends or family if they were experiencing similar pain.

#### *Questions relating to functional movement therapy*

78% participated in specific and distinctive skill acquisition functional movement therapy. 22% did not. Patients who did not utilise functional movement therapy in conjunction with ketamine all described no qualitative improvement in pain.

#### *Questions relating to side effects and tolerance*

Overall, 26% described a symptom that they felt was a side effect of ketamine. 63% described no side effects at all. 11% were uncertain. Of the 26% that described side effects approximately half felt that they were minor enough to continue ketamine use. The remaining half amounting to approximately 13% of patients did cease ketamine because of perceived side effects. The range of side effects from major to minor, respectively included suicidal ideations, worsening depression, sedation, dizziness, foggy brain and poor concentration amongst other minor symptoms associated with all pharmaceuticals. Interestingly suicidal ideations and depression side effects reported in our series are emerging additional indications for ketamine use [33].

Our results show very high efficacy comprised of distinctive improvement in chronic pain symptoms in a cohort of patients with severe pain and disability most of whom had exhausted alternative pain medication and management options recruited from a tertiary care setting. The tolerance and safety profile were also favourable with only 13% of patients deciding to cease ketamine because of side effects.

## Discussion

Our retrospective analysis of the utility of ketamine in 108 patients with significant elements of defined central functional chronic low back pain represents the largest published series to date. Aside from the reported efficacy and safety of ketamine applied with our cause (movement dysfunction) and pain symptom focused clinical model, addressing causation with functional movement therapy and diagnosing pain symptoms in the framework of peripheral structural pain and central functional pain, numerous pertinent issues have emerged through our research that require broader application to more effectively address the growing epidemic of chronic low back pain observable in industrialised nations.

Currently a cause-based clinical model is lacking in regard to the symptoms of chronic low back pain. Broadly cited articles go as far as to claim there is no patho-anatomical cause for low back pain, instead preferencing the term nonspecific low back pain [34]. We find this remarkable given that low back pain is so ubiquitous and prevalent and as such a common causation or disease, by definition must exist. To deny existence of a cause, destines treatment paradigms to purely symptom focused approaches. Addressing symptoms alone is a fundamentally flawed paradigm with predictable ultimate failure.

We have adopted a cause focused clinical model based on biomechanical movement dysfunction defined by poor expression of hip centric spino-pelvic rotation, neutral spine awareness and maintenance and compromised posterior kinetic chain powered movement [18–20,23,25,26]. This represents poor bending proficiency, injurious for evolutionary bipedal humans maintaining the unevolved spino-pelvic morphology of our quadrupedal ancestors [35]. Movement Dysfunction drives biomechanical stress into the lumbar motion segments, particularly L4/5 and L5/S1. Biomechanical stress drives biological inflammation and nociception that accumulatively results in pain, disability and progressive premature structural break down observable as degeneritis or spondylitis. Degeneritis and spondylitis is distinct from degeneration or spondylosis which is a normal pain free ageing process devoid of inflammatory or nociceptive pain or disability. Defining a movement dysfunction cause permits delivery of a specific movement therapy intervention that restores movement proficiency [19,26].

A clear framework of pain symptoms needs to be applied to the elements of chronic low back pain in order to select appropriate symptom focused interventions. Similar to selecting the appropriate antibiotic for the bacterial infection appropriate pain interventions must also be tailored to the clinical presentation.

On one end of the spectrum of pain symptoms a purely peripheral structural pain such as symptomatic instability which would be expected to resolve with stabilising surgery. The other end of the spectrum may be represented by severe persisting low back pain and disability years after a minor trauma with normal spinal imaging reflecting dominant central functional pain.

Any combination of peripheral structural pain and central functional pain may coexist demanding equal attention. There is no dictate that a patient with chronic spinal instability related symptoms cannot also be experiencing secondary symptoms of central functional pain [6,17].

This clinical model may explain the frequency of what is termed Failed Back Pain Surgery Syndrome - uncomplicated spinal stabilising surgery (fusion or disc arthroplasty) that fails to resolve back pain symptoms. Historically this might be regarded as inappropriate surgical treatment of a non-significant structural pain generator [36,37]. The structural target of surgery may have required intervention; however it exposes in these patients who receive routine uncomplicated surgery that a mechanism for pain exists beyond the treatment capacity of the purely structural intervention of surgical stabilisation. If pain can only be structural or functional in origin and the significant structural pain generators are eliminated (through surgery in this cohort), only central functional pain remains to be treated. If central functional pain was addressed prior to the spinal stabilising surgery, it may have in fact mitigated the requirement for surgery altogether. If it is effectively addressed, after surgery for persisting pain, improvement can be expected as demonstrated in our cohort of post-surgical patients.

Our cohort of patients would be classified as severely affected given the chronicity of symptoms and failure of primary and secondary care. All patients were recruited *via* a tertiary care specialist service thus biasing our results towards poor outcomes. Despite this the improvements observed were of high clinical significance. The presence of central functional pain elements in patients with chronic pain reinforces the importance of early and effective treatment of low back pain in the acute stages to mitigate the development and manifestation of secondary neurological central functional pain on top of peripheral structural pain induced by a mechanical injury. By inference early effective anti-inflammatories and nociceptive analgesia in combination with functional movement therapy is extrapolated to be the optimal first line intervention for low back pain in the acute and sub-acute stages given that this approach resolves perpetuating causation, simultaneously with structural pain symptoms. This prevents the development of more challenging and entrenched central functional pain patho-neurophysiology. Acutely painful structural injuries are permitted to comprehensively heal in the expected time frame without the development of central sensitisation and chronicity [21,22].

Ketamine inhibits action on the excitatory NMDA receptor and has crossover associations with alteration to memory. If central functional pain is conceptualised as a "memory of pain" without ongoing legitimate structural compromise the clinical model of separating peripheral structural pain from central functional pain becomes more valid. Memories can only be a neurological construct and so memories of pain will never be resolved with structural interventions. Neurobiological research has shown NMDA receptor hypofunction has association with decreased memory and dementia. Therefore, a logical mechanism of action exists for ketamine to suppress neurological memories of pain that we regard as central functional pain [31].

Our results reflect and support our clinical model for chronic low back pain. Poor outcomes were mostly restricted to patients who did not comply with cause focused movement therapy rehabilitation. In these individuals the causation stimulus for central functional pain persists even in the face of compliant ketamine use.

Ketamine is utilised selectively for chronic low back pain management however most experience and protocols are parenteral with short inpatient periods of intravenous infusion (seven days), behaving as a pain circuit breaker [38–40]. We feel that the utility of such intervention is limited given that central functional pain remains a chronic condition and as such requires equally chronic outpatient symptom and cause focused treatment. The Sublingual ketamine troche formulation we used which is widely obtainable has proven to be safe, efficacious, affordable and practical for this purpose.

## Conclusion

With chronicity the likelihood of central functional pain contributing to the overall pain experience increases and the initial presentation of peripheral structural pain, mostly resolved, transforms into one dominated by central functional pain. In our observation Ketamine has the potential to assist significantly in 80% of appropriately selected patients managed simultaneously with functional movement therapy. Failed Back Pain Surgery Syndrome may not be a reflection of failed surgery per se but a failure to address underlying central functional pain. Ketamine is safe and efficacious for outpatient sublingual consumption in patients with designated central functional back pain. The dosage required is low compared to limited utility inpatient continuous intravenous or subcutaneous infusions. The side effect profile is well tolerated. Ketamine's effectiveness appears to be dependent on the simultaneous application of Functional Movement Therapy by way of distinctively mitigating ascending peripheral structural pain stimuli in a way that other forms of common physical rehabilitation such as core strengthening, stretching and manual therapy neglect. Central Functional Pain characterised by allodynia and hyperalgesia conceptualised as a functional neurological disorder or even as a chronic memory of pain is distinct from peripheral structural pain comprised of inflammation, nociception and neuropathic pain. As such central functional pain is more challenging to resolve but as shown in our series able to be effectively treated utilising a distinctive cause and symptom focused intervention.

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