AUCTORES
Globalize your Research

Journal of Brain and Neurological Disorders
Rehan Haider *

Open Access

Research Article

# Brain Cells Act Like a Volume Knob for Arousal and Pain Control

**Rehan Haider [1]*, Hina Abbas [2], Shabana Naz Shah [3]**

[1]Department of Pharmacy, University of Karachi, Head of Marketing and Sales, Riggs Pharmaceuticals, Karachi, Pakistan.

[2]FCPS fellow college of Physician and surgeon, Department of Pathology, Dow University of Health Sciences, Karachi, Pakistan.

[3]Pharmaceutical chemistry Faculty of Pharmacy, SBB Dewan university Karachi Pakistan.

***Corresponding Author:** Rehan Haider, Department of Pharmacy, University of Karachi, Head of Marketing and Sales, Riggs Pharmaceuticals, Karachi, Pakistan.

**Received Date:** December 22, 2025 | **Accepted Date:** December 30, 2025 | **Published Date:** January 07, 2026

**Citation:** Rehan Haider, Hina Abbas, Shabana N. Shah, (2026), Brain Cells Act Like a Volume Knob for Arousal and Pain Control, *J. Brain and Neurological Disorders*, 9(1): **DOI:10.31579/2642-973X/165**



## Abstract

Arousal and pain are braided by highly regulated mechanisms for brain function that enable organisms to show the right thing towards different stimuli, both inside and outside their body. There have been novel findings concerning the workings of certain brain cells that work similarly to a "volume knob," modulating arousal and pain intensity rather than working as a switch that turns on and off to signal arousal and pain sensation to the organism. The brain cells primarily responsible for this modulation mechanism include the Noradrenergic cells of the locus coeruleus, Serotonergic cells of the raphe nuclei, Cholinergic cells of the basal forebrain, and the Inhibitory interneurons of the thalamus and the cortex.

Experimental studies in animal models and human brain imaging studies show that activation and modulation of these neuronal groups could enhance or reduce pain perception, together with modulation of alertness, attention, and stress response. The dysfunction of this 'neural volume control' system has also been linked to chronic pain conditions, sleep disturbance, anxiety, and depression, which makes this system highly relevant in clinical conditions. The modulation of brain cells in this continuum could provide novel knowledge in brain and body integration, besides offering promising ways in which pain modulation could be made in those conditions.

This paper integrates existing knowledge on cellular and circuit-based neural processes behind the linking of arousal and pain, and it also reviews methodologies employed in experimental studies focusing on these processes. This research plays an important role in affecting a transition to new ideas in understanding brain regulation processes because it presents these processes in a non-binary format.

**Key Words:** arousal; pain modulation; neuromodulation; locus coeruleus; thalamus

## Introduction

Functions of arousal and pain are basic neurobiological phenomena that are critical to maintaining life and are involved in adaptive reactions to danger and endogenous disturbances. Classically, these phenomena could be viewed as distinct states; recently, however, there is a growing body of evidence to suggest that their function is to control a continuum and are modulated by a type of brain cell that is responsible for the modulation of intensity level rather than just the presence or absence of a signal, akin to a "volume knob" to turn up or turn down experience as appropriate to the context.

A key aspect of this regulation is the use of neuromodulatory systems, such as noradrenergic, serotonergic, dopaminergic, and cholinergic projections, which have a broad pattern of regulation of cortical and subcortical areas [4,5]. The interactions of these systems with pain-regulating systems in the spinal cord, thalamus, and limbic and cortical areas play a pivotal part in the regulation of the sensory and emotional aspects of pain perception [6,7]. The knowledge of this integrated regulation is essential for treating conditions associated with dysregulated arousal states and pain sensitivity patterns [8].

## Literature Review

### Arousal Regulation with Neuromod

The locus coeruleus-norepinephrine system also prominently regulates arousal and attention by manipulating gain in neural networks [9]. Tonic firing increases arousal or alertness, while phasic firing improves stimulus-related responses [10].

### Pain Modulation and Neural Gain

Pain sensation is also significantly affected by the brain stem and cortical circuitries that regulate the nociception transmission [11]. The inhibitory and facilitatory pathways help to regulate the intensity of pain [12].

### Shared Circuits for Arousal and Pain

In addition to their involvement in arousal regulation, the following are some key shared neural components between arousal and pain regulation: thalamus, anterior cingulate cortex, and insula [13,14]. The shared components are also responsible for the augmentation of intensities of pain triggered by arousal and therefore-induced reduction in sensitivity to pain by sed.

### Research Methodology

For the purposes of the review, a structured literature search of biomedical journals was conducted. The preferred methodology included experimental works done in the use of animal models, human neuroimaging, electrophysiology, and optogenetics. The inclusion criteria for the review involved the use of research that explored graded neural control of either arousal or pain.

## Statistical Analysis

Among the quantitative studies reviewed, the typical methods for associating neuronal activity with behavioral or physiological measures included correlation analysis, linear mixed-effects models, and multivariate regression. Neuroimaging studies commonly utilize some form of voxel-wise analyses corrected for multiple comparisons. Significance was typically set at $p < 0.05$.

## Results

These effects were proportional across studies, with graded activation of neuromodulatory neurons leading to matching changes in arousal and pain sensitivity. In this way, increased noradrenergic or cholinergic tone augmented alertness and pain responsiveness, whereas decreased activity reduced both dimensions [17–19]. Importantly, these effects were dose-dependent, supporting the “volume knob” model.

| Brain Region | Cell Type / Neurotransmitter | Primary Function | Effect on Arousal | Effect on Pain Perception |
|---|---|---|---|---|
| Locus Coeruleus | Noradrenergic neurons | Neural gain modulation | Increases alertness and vigilance | Amplifies or suppresses pain depending on firing mode |
| Raphe Nuclei | Serotonergic neurons | Mood and sensory regulation | Stabilizes arousal states | Modulates descending pain inhibition |
| Basal Forebrain | Cholinergic neurons | Attention and cortical activation | Enhances wakefulness | Alters pain sensitivity via cortical processing |
| Thalamus | GABAergic interneurons | Sensory gating | Regulates sensory throughput | Filters nociceptive signals |
| Anterior Cingulate Cortex | Pyramidal neurons | Emotional pain processing | Heightens arousal under stress | Influences affective pain dimension |
| Insular Cortex | Multimodal neurons | Interoceptive awareness | Integrates bodily arousal | Scales subjective pain intensity |

**Table 1:** Key Brain Cell Populations Involved in Graded Regulation of Arousal and Pain

| Methodology | Model/System | Measured Outcome | Key Insight |
|---|---|---|---|
| Optogenetics | Rodent models | Neuronal firing rates | Dose-dependent control of arousal and pain |
| fMRI | Human subjects | BOLD signal changes | Correlation between arousal circuits and pain intensity |
| Electrophysiology | Animal and human | Synaptic activity | Neural gain adjustment |
| Behavioral assays | Rodent pain models | Withdrawal thresholds | Graded pain modulation |
| Pharmacological modulation | Clinical/experimental | Neurotransmitter levels | Scalable changes in perception |

**Table 2:** Experimental Approaches Used to Study Neural “Volume Control” Mechanisms

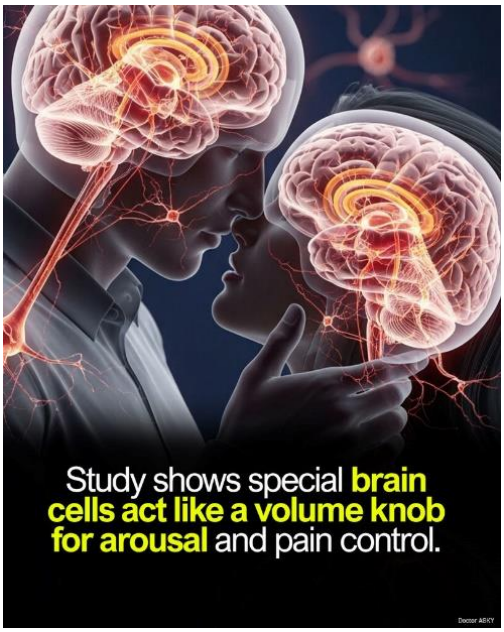


**Figure 1:** Neural "Volume Knob" Model of Arousal and Pain Regulation

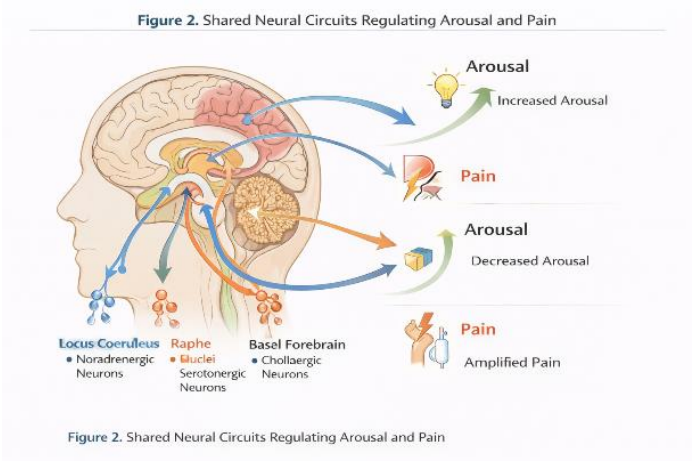


**Figure 2:** Shared Neural Circuits Regulating Arousal and Pain

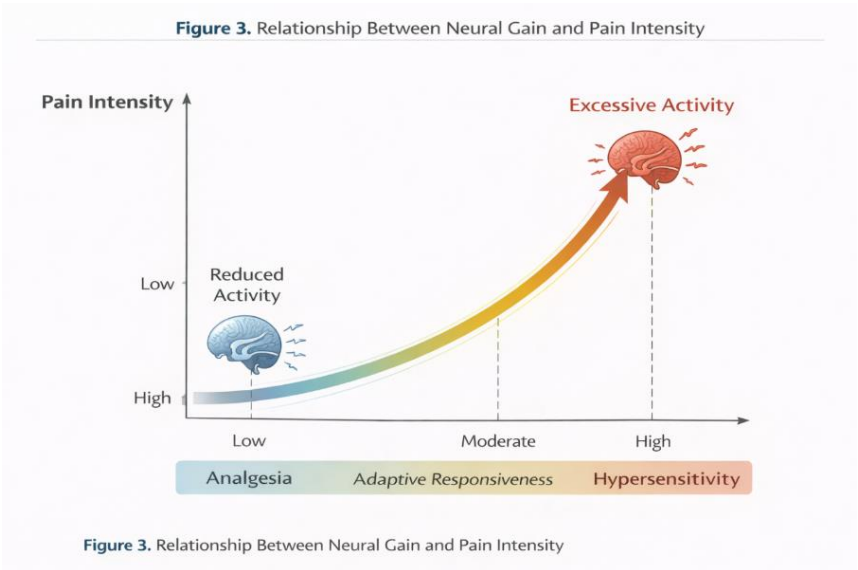


**Figure 3:** Relationship Between Neural Gain and Pain Intensity

## Discussion

These findings support a paradigm wherein brain cells manage arousal and pain through scalable modulation rather than binary switching. The framework elucidates individual variability in pain sensitivity and vulnerability to stress-related disorders [20]. It would further imply that therapeutic strategies aimed at neural gain-neuromodulation, mindfulness, and precision pharmacology may prove more effective than traditional analgesics [21–23].

## Conclusion

Brain cells function rather like an automatic volume control mechanism with regard to arousability and pain, in which they modulate inputs in order to adjust to specific stimuli. The realization that this type of modulation exists has brought with it a greater understanding of brain cell function and new approaches for alleviating cases of chronic pain and arousability.

## Acknowledgments

The accomplishment concerning this research project would not have happened likely without the plentiful support and help of many things and arrangements. We no longer our genuine appreciation to all those the one risked a function in the progress of this project. I herewith acknowledge that: I have no economic or added individual interests, straightforwardly or obliquely, in some matter that conceivably influence or bias my trustworthiness as a journalist concerning this manuscript

**Conflicts of Interest:** The authors declare that they have no conflicts of interest.

**Financial Support and Protection:** No external funding for a project was taken to assist with the preparation of this manuscript

## References

1. McGinley MJ, et al. (2015). *Neuron*.; 87:1143–1161.
2. Aston-Jones G, Cohen JD. (2005). *Annu Rev Neurosci*.; 28:403–450.
3. Sara SJ. (2009). *Nat Rev Neurosci*.; 10:211–223.
4. Bouret S, Sara SJ. (2005). *Trends Neurosci*.; 28:574–582.
5. Sarter M, et al. (2009). *Brain Res Rev*.; 59:1–16.
6. Fields HL. (2004). *Nat Rev Neurosci*.; 5:565–575.
7. Apkarian AV, et al. (2005). *Nat Rev Neurosci*.; 6:463–475.
8. Wiech K. (2016). *Nat Rev Neurosci*.; 17:154–162.
9. Berridge CW, Waterhouse BD. (2003). *Brain Res Rev*.; 42:33–84.
10. Devilbiss DM, Waterhouse BD. (2011). *J Neurosci*.; 31:6817–6826.
11. Heinricher MM, et al. (2009). *Brain Res Rev*.; 60:214–228.
12. Ossipov MH, et al. (2010). *Nat Rev Neurosci*.; 11:682–693.
13. Craig AD. (2009). *Nat Rev Neurosci*.; 10:59–70.
14. Bushnell MC, et al. (2013). *J Neurosci*.; 33:1813–1823.
15. Woo CW, et al. (2017). *Nat Commun*.; 8:1–11.
16. Friston KJ. (2011). *Neuroimage*.; 56:1–13.
17. Martins AR, Froemke RC. (2015). *Nat Neurosci*.; 18:1649–1657.
18. Loggia ML, et al. (2014). *Brain*.; 137:3011–3020.
19. Maniscalco JW, Rinzel J. (2013). *J Neurosci*.; 33:2005–2017.
20. Tracey I, Mantyh PW. (2007). *Neuron*.; 55:377–391.
21. Garcia-Larrea L, Peyron R. (2013). *Lancet Neurol*.;12:629–641.
22. Ossipov MH. (2012). *Pain*.; 153:1147–1158.
23. Bushnell MC, et al. (2013). *Pain*.;154: S12–S20.
24. Seymour B. (2019). *Nat Rev Neurosci*.; 20:747–760.
25. Baliki MN, Apkarian AV. (2015). *Neuron*.; 87:4.



**DOI:10.31579/2642-973X/165**