



OPEN Quantitative assessment of lumbar dural mater pulsations using granger causality testing for spinal dynamics

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Spinal disorders lead to paralysis, numbness, pain, etc., due to nerve compression within the spinal canal, affecting quality of life (QOL). Identifying nerve compression is vital for accurate diagnosis. The pulsation of the dura mater, which contains cerebrospinal fluid (CSF) from the choroid plexus, is sometimes evaluated with ultrasound during surgery. Despite its clinical relevance, the physical characteristics of this pulsation remain largely unexplored due to advancements questioning traditional bulk flow theories. This study aimed to analyze the dynamics of dura mater pulsation for a better understanding of these characteristics. Dura mater pulsation was captured using ultrasound at the lumbar spine level in healthy volunteers lying prone. Simultaneously, electrocardiography (ECG), respiratory volume, and respiratory motion were measured. Seasonal Trend Loess (STL) decomposition was employed to decompose the seasonal trends of respiratory and cardiac cycles for comparison with ECG and respiratory data. Both time and frequency domain analyses were conducted, and causal relationships were estimated using Granger causality. The seasonal components of both the respiratory cycle and respiration, as well as the cardiac cycle and heartbeats, exhibited matched spectral peaks and periodicity. Plotting the original dura mater pulsation waveform and the residual component spectra revealed a decreasing trend resembling the $1/f$ fluctuations typical of vital signals such as heartbeats. While no direct causal relationship between respiration, heartbeats, and dura mater pulsation was found, Granger causality was demonstrated by extracting cardiac and respiratory cycle components from the dura mater pulsation using STL decomposition. The presence of Granger causality between the seasonal components of the respiratory and cardiac cycles and dura mater pulsation implies their interrelated dynamics. However, the absence of direct causality between respiration, heartbeats, and dura mater pulsation, combined with the complex nature of vital signals indicated by $1/f$ fluctuations in the residual components, necessitates focused analyses on specific periods.

Keywords Dural mater, CSF (cerebrospinal fluid), Dynamics, Ultrasound, Lumbar, Lumbar spinal stenosis

In developed countries with aging populations, musculoskeletal disorders, including chronic back and joint pain, are prevalent¹. Spinal disorders such as degenerative spondylosis and spondylolisthesis cause symptoms from neural tissue compression in the spinal canal, affecting Activities of Daily Living (ADL) and Quality of Life (QOL)²⁻⁵. Therefore, identifying the intracanal pathologies, including nerve compression, is crucial in diagnosing and treating these disorders. The spinal cord and cauda equina are encased in dura mater and bathed in cerebrospinal fluid (CSF)⁶. It is qualitatively known that the dura mater exhibits pulsations roughly synchronized

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with the heartbeat, corresponding to the dynamics of the CSF inside. Dural pulsation indicates that the spinal cord is free within the subarachnoid space and free from extrinsic compression and is qualitatively evaluated in clinical practice. While the detailed characteristics of these pulsations remain unclear, CSF, once dubbed the "third circulation," is under scrutiny, with new insights challenging the Bulk Flow theory of CSF movement^{7–10}. Recent real-time MRI studies provide compelling evidence that inspiration is the primary regulator of CSF flow in humans. During forced breathing, CSF flow significantly increases during each inspiration, while breath-holding suppresses it almost entirely. Inspiratory thoracic pressure reduction plays a critical role in modulating CSF dynamics by influencing the CSF pressure gradient along clearance pathways^{11,19}. For instance, it is known that even after removing the choroid plexus, which is responsible for CSF production, most of CSF production is maintained⁹. Research by Oreskovic and others has demonstrated that CSF production occurs from the choroid plexus and brain capillaries¹⁰. Furthermore, studies by Weed and McComb discovered that CSF is absorbed through the arachnoid granulations only when intracranial pressure reaches high levels (around 150 mmHg). When intracranial pressure is maintained within normal limits, CSF is absorbed through the nasal lymphatics^{12,13}. Di Chiro et al., using RI brain cisternography via lumbar puncture, traced the movement of CSF and described that only about 1/5 to 1/3 of CSF is absorbed through arachnoid granulations via Bulk Flow. In contrast, the majority is absorbed through capillaries throughout the brain tissue¹⁴. Thus, in recent years, there have been various suggestions regarding the mechanisms of CSF production and absorption. As a tracer-free technique for tracing cerebrospinal fluid (CSF), the MRI Time-SLIP (Time-spatial labeling inversion pulse) method exists. By labeling CSF itself as an endogenous tracer, it is possible to understand the true dynamics of CSF without the influence of tracer molecule diffusion¹⁵. Yamada et al. using this technique have reported various dynamics of CSF. In the normal subarachnoid space of the spine, CSF exhibits small amplitude pulsations synchronized with heartbeat and large amplitude pulsations synchronized with respiration. However, due to the presence of these two driving forces, the physiological dynamics of CSF do not exhibit complete repeatability or reproducibility^{16–18}.

The current study aimed to quantitatively assess and elucidate the origins and dynamics of dura mater pulsation, comparing it with cardiac and respiratory activity.

Results

STL and seasonal components

Figure 1A shows the frequency spectrum of the original waveform of dura mater pulsation before STL decomposition.

The original waveform of dura mater pulsation exhibited a large spectrum in the low-frequency domain, with a noticeable attenuation in spectral strength towards higher frequencies. Furthermore, it did not show specific spectral peaks but had peaks in multiple frequency spectra, indicating a composition of multiple periodic components. Additionally, the logarithmic plot of the spectrum exhibited a right-declined behavior, characteristic of the $1/f$ fluctuation, a characteristic where power is stronger at lower frequencies and weaker at higher frequencies, commonly observed in biological signals such as heartbeat.

Figure 1B shows the results for dura movement of a single subject.

Figure 2 shows the seasonal components of dural pulsations after seasonal decomposition based on the respiration cycle (seasonal_res), along with the waveforms of respiratory flow volume (res_volume) and respiratory movement (res_move).

Figure 3 shows the spectrum analysis results of these waveforms in the frequency domain.

While there were variations in respiratory cycles among subjects, both respiratory flow volume and respiratory motion exhibited main spectral peaks within the normal respiratory frequency range (0.2–0.33 Hz). Within the same subject, the main spectral peaks of respiratory motion and its seasonal variation coincided. It indicates that the seasonal component of respiratory cycles was accurately captured using STL. Respiratory flow volume and respiratory motion exhibited the same cycle but with phase differences. Similarly, phase differences were observed in their seasonal variations. These phase differences are considered to be caused by errors in measurement positions, as respiratory volume changes follow chest movements, and respiratory motion is measured at the chest. In contrast, dura mater pulsation is measured at the lumbar region.

Figure 4 shows the seasonal components of dural pulsations after seasonal decomposition based on the heartbeat cycle (seasonal_hb) and the electrocardiogram (ECG) waveform.

Figure 5 presents the spectrum analysis results of these waveforms in the frequency domain.

In spectral analysis, main spectral peaks within the normal heart rate frequency range (1.0–1.67 Hz) were observed for all examiners, despite differences between them. The main spectral peak positions of ECG and dura mater pulsation heart rate seasonal variation were aligned for the same examiner. Therefore, the seasonal variation of heart rate was believed to be accurately captured using STL.

Figure 6 shows the spectrum of residual components after performing STL decomposition on respiration and heartbeat and removing seasonal variations and trend components.

This result is based on a single representative measurement. Since there are variations depending on the measurement location and the subject, Granger causality estimation is utilized to comprehensively evaluate all measurement results and ensure the robustness of the findings.

Granger causality test

We focused on the causality between the seasonal components separated by STL (seasonal_res, seasonal_hb), the respiratory, and the ECG. The pulsation of the dura mater was decomposed into seasonal components by STL decomposition, revealing Granger causality with ECG and res_move. Although the causal relationship between ECG and dural pulsation cannot exclude the influence of pulsation from blood vessels around the dura mater, the results satisfy Monroe Kelly's law. Changes in arterial blood flow synchronized with the heartbeat cycle act

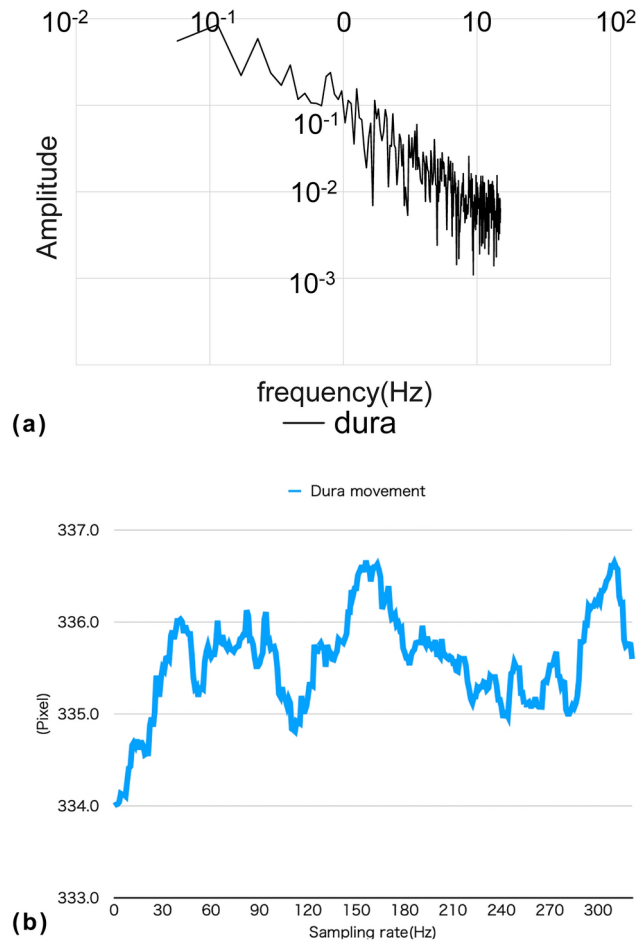


Fig. 1. The spectrum of dura mater pulsation. Plotted on both logarithmic axes.

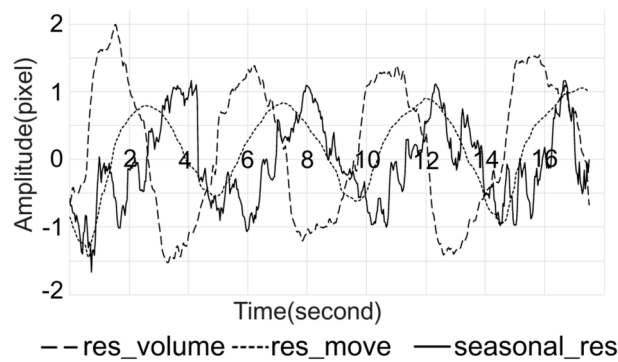


Fig. 2. Measured respiratory waveform and respiratory cycle seasonal component of dura mater. Respiratory volume: res_volume. Respiratory movement: res_move. Respiratory cycle seasonal component of dura mater: seasonal_res.

on the CSF as pressure waves, supporting the relationship between pulsation (heartbeat) and respiration as described by Monroe Kelly’s law. These findings align with the prevailing view that the influx of arterial blood to the cranium during systole drives CSF movement from the cranium to the spine to satisfy the Monroe-Kelly doctrine. The results support Monroe Kelly’s kinetics, which has become the mainstream view in recent years, rather than the conventional bulk flow kinetics related to cerebrospinal fluid production and resorption. However, the mechanism of production and resorption itself has not been ruled out.

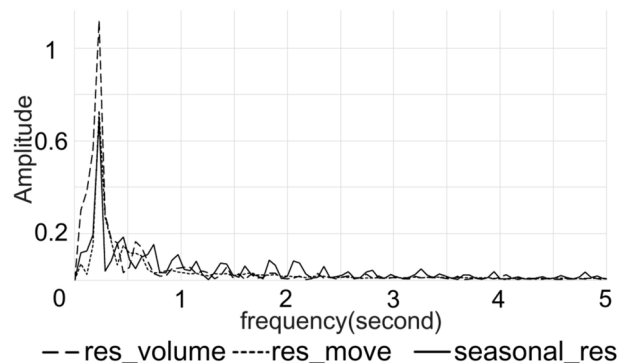


Fig. 3. The spectrum of respiration and respiratory cycle seasonal component of dura mater. The spectrum of respiratory volume: *res_volume*. The spectrum of respiratory movement: *res_move*. The spectrum of respiratory cycle seasonal component of dura mater: *seasonal_res*.

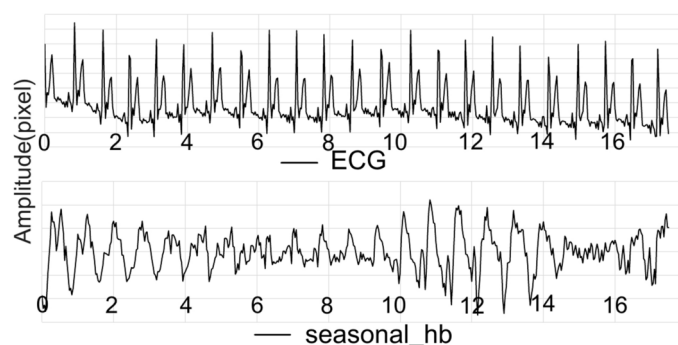


Fig. 4. Measured ECG waveform and heartbeat cycle seasonal component of dura mater. Heartbeat cycle seasonal component of dura mater: *seasonal_hb*.

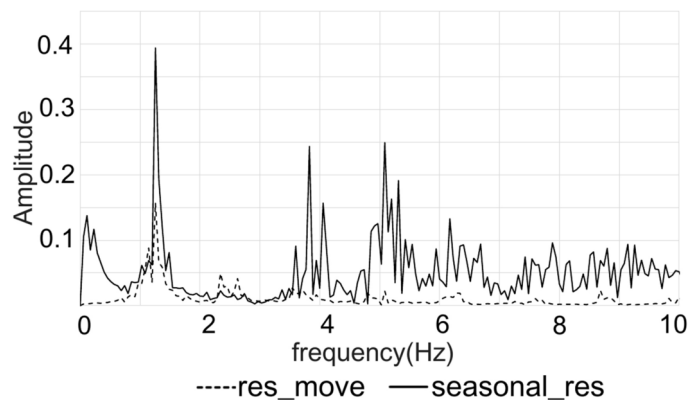


Fig. 5. The spectrum of ECG and heartbeat cycle seasonal component of dura mater. The spectrum of heartbeat cycle seasonal component of dura mater: *seasonal_hb*.

Discussion

We found that the pulsation of the dural canal exhibits $1/f$ fluctuation. Using STL decomposition, we extracted the components of heartbeat and respiratory cycle fluctuations from multiple periodic fluctuations and performed the Granger causality test. Although direct Granger causality between dural tube pulsation and heart rate or respiration was not established, some causal relationships were found through seasonal decomposition.

STL and seasonal components

Assuming that dura mater pulsations are composed solely of seasonal variations in respiratory and cardiac cycle periods, as well as trend variations, the residual components after STL decomposition should consist of

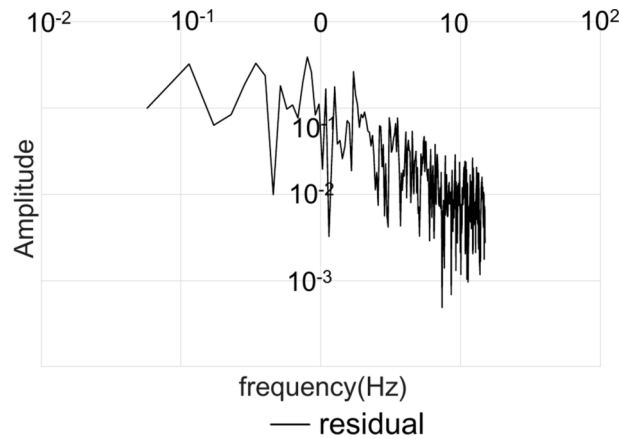


Fig. 6. Residual components of the dural canal beat after STL decomposition. Plotted on both logarithmic axes.

temporally independent and completely random components, along with specific outliers or singular influences, which should be extremely small in magnitude. However, multiple spectra and significant power remain in the residual components after decomposing the respiratory and cardiac cycles as seasonal periods. This indicates the presence of additional variations in dura mater pulsations beyond those associated with the cardiac and respiratory cycles. When plotted on a logarithmic scale, the residual component of dura mater pulsations exhibits an overall right-declined behavior in the spectrum, similar to the original waveform of the dura mater. The spectrum near the respiratory and heartbeat frequencies, separated by STL decomposition, is minimized due to the removal accomplished by the STL decomposition. Therefore, the pulsation of the dura mater also exhibits a $1/f$ fluctuation similar to other biological signals, such as the heartbeat, and includes components synchronized with the heartbeat and respiration.

Granger causality test

The expected causal relationships were not sufficiently confirmed in the current study. Previous studies suggested that the dynamics of CSF are governed by body movements, such as respiration, and are significantly perturbed. In the current study, participants were measured in a supine position under resting conditions, where the primary movements were the fluctuations associated with respiration. Granger causality was observed between respiratory movement (*res_move*) and the seasonal components of the pulsation of the dura mater, providing evidence for the presence of dynamics driven by this bodily movement, particularly respiration. On the other hand, causality between respiration volume (*res_volume*) and dura mater pulsation was not established. The Granger causality test can only estimate direct causality and does not account for the influence of confounding variables. Respiration flow volume (*res_volume*) is a phenomenon induced by respiratory movement (*res_move*), which has been shown to have causality with heartbeats. Additionally, *res_move* is also influenced by heartbeats. Therefore, many confounding relationships exist between respiration volume and dura mater pulsation. Consequently, no causality was observed with respect to *res_volume*. When discussing causality between respiration and dura mater movement, it should be taken into account that the primary effect of respiration is associated with shifts of blood in the venous system¹⁹. The filling of epidural veins and changes in venous volume in the head can lead to shifts in the cerebrospinal fluid (CSF), resulting in dura mater movements through the filling and emptying of CSF in the subarachnoid space of the spine.

One possible reason for this finding is the presence of various cyclic fluctuations in the pulsation of the dura mater due to the inherent $1/f$ fluctuations in biological signals. The dynamics of this process are not simple, which may explain why a straightforward causality between respiratory volume and dura mater movement was not observed. Biological signals generally manifest due to the complex interplay of multiple physiological phenomena. Granger causality estimation is limited in its ability to account for confounding relationships and demonstrate causality in biological signals with many confounding factors. Therefore, to accurately elucidate causality in biological signals with multiple confounding factors, it is necessary to consider alternative methods and enrich domain knowledge, such as anatomical insights.

Although direct causality between heartbeat, respiration, and dural pulsation was not demonstrated in the current study, causality could be established in some waveforms after seasonal adjustment, suggesting the possibility that dural pulsation may have cardiac and respiratory properties. Previous studies by Yamada et al. reported cardiac and respiratory properties of cerebrospinal fluid pulsation, but the current study was able to quantitatively demonstrate these properties^{16–18}. Furthermore, it was discovered that the pulsation of the dura mater exhibits $1/f$ fluctuations. Biological signals with $1/f$ fluctuations, such as heart rate, have been applied in various diagnoses by focusing on specific periods or cycles for measurement and analysis^{20–22}. The pulsation of the dura mater, like other biological signals with $1/f$ fluctuations such as heartbeats, may yield new insights when analyzed focusing on specific periods or cycles.

In Kimura et al.'s study, similar to the present research, they attempted quantitative analysis of dural mater pulsation using ultrasound. They investigated the relationship between the empirically known amplitude of dural

pulsation and the degree of spinal cord decompression, demonstrating that spinal cord pulsation amplitude significantly differs depending on the decompression status of the spinal cord^{16–18}.

In previous studies by Yamada et al.^{16–18}, similar to the current study, they attempted quantitative analysis of dura mater pulsation using ultrasound. They investigated the relationship between the empirically known amplitude of dural pulsation and the degree of spinal cord decompression, demonstrating that spinal cord pulsation amplitude significantly differs depending on the decompression status of the spinal cord. In previous studies by Yamada et al., it was qualitatively found that CSF flow is obstructed at the site of stenosis in patients with spinal canal stenosis. In the current study, we aimed to quantitatively demonstrate the standard of dural pulsation by analyzing healthy individuals without compression. However, as suggested by previous research, the nature of dural pulsation in patients with stenosis may differ. Therefore, conducting analyses not only on healthy individuals but also on various spinal disorders and comparing them may be meaningful. The current study suggests a novel basic approach to consider dural pulsation, which has not been previously considered, opening up new avenues for investigation. Incorporating recent findings from real-time MRI studies, which highlight the critical role of inspiratory thoracic pressure reduction in regulating CSF flow, future research should compare these dynamics in normal and pathological states, such as spinal canal stenosis. This could lead to a better understanding of how impaired thoracic pressure modulation affects CSF dynamics and clearance pathways.

The current study has some limitations.

First, Ultrasound imaging of the dura mater is challenging due to acoustic shadows caused by surrounding bone tissue, which limits imaging angles and positions. These imaging difficulties result in variations in quality between subjects, making it difficult to maintain experimental consistency. Second, The small sample size of six subjects restricts the ability to generalize the findings to broader contexts. To define the characteristics of dural pulsation more generally, analysis with a larger number of subjects is necessary. For example, Kimura et al. attempted to analyze dural pulsation using ultrasound and studied 85 patients. Therefore, it is desirable to secure a similar number of subjects in this study as well. Thirdly, the pulse extraction method limits the measurement time to approximately 20 s, reducing reliability for low-frequency analysis. Therefore, in the current study, the measurement time is limited to approximately 20 s, leading to reduced reliability of low-frequency domain analysis using Fourier analysis. Additionally, in a previous study by Yamada et al.^{16–18} using MRI Time-SLIP method, the observation time was also short, lasting only a few seconds. Establishing a method capable of longer-term measurements may be necessary for a more detailed and accurate analysis of dural pulsation. Finally, while respiratory flow and displacement are inherently related and could confound the causality analysis, their inclusion was deemed necessary for modeling the system's dynamics in this study. To address this, STL decomposition was employed to mitigate periodic respiratory and cardiac influences, isolating the residuals for further analysis. However, we recognize this as a limitation of the current approach. Future studies should aim to refine the causality assessment by excluding respiratory variables to avoid potential confounding effects and further improve the robustness of the analysis.

In conclusion, the presence of Granger causality between the seasonal components of the respiratory and cardiac cycles and dura mater pulsation implies their interrelated dynamics. However, the absence of direct causality between respiration, heartbeats, and dura mater pulsation, combined with the complex nature of vital signals indicated by $1/f$ fluctuations in the residual components, necessitates focused analyses on specific periods.

Method

Participants

The participants are six healthy volunteers (average age 23.3 ± 0.51 years) with no history of previous spinal trauma, surgery, or neurological disorders. Eighteen interlaminar spaces in total were investigated, with three locations examined per individual.

Experiment

All procedures were performed in accordance with relevant guidelines/regulations with enough informed consent obtained from all participants and/or their legal guardians in accordance with the Declaration of Helsinki.

In this study, we assumed that dural pulsations are composed of multiple periodic waveform components, particularly influenced by heartbeats and respiration. Therefore, we employed Fourier analysis to identify the frequency characteristics of dural pulsations. Furthermore, using seasonal decomposition (STL: Seasonal Trend decomposition using Loess²³), we extracted the variations in heartbeats and respiration cycles and compared them with simultaneously measured heartbeats and respiration. Additionally, to quantitatively estimate the causal relationship between dural pulsations and heartbeats/respiration, we investigated the causal relationships between dural pulsations and heartbeats/respiration using the Granger causality test, a statistical hypothesis test. Below, we describe the analysis and measurement methods conducted for each.

Measurement

The pulsations of the dura mater were recorded as dynamic images using the Applio500 ultrasound device (Canon Medical Systems Inc., Tokyo, Japan). The probe used for this purpose was the convex probe PVT-375B (Canon Medical Systems Inc., Tokyo, Japan). The sampling rate for ultrasound is 30 Hz. Subjects were placed in a prone position, and the probe was applied axially to the lumbar region at a higher level. Imaging was performed to capture axial images, with particular attention paid to the positioning and angle of the probe. The dura mater is surrounded by vertebral tissues with high acoustic reflectivity, making it prone to hiding behind acoustic shadows such as vertebral arch (Fig. 7). Using the spinous process as a reference point, we identified the area within the spinal canal that exhibited a pulsation distinct from its surroundings as the dura mater, marking this spot with a red ellipse. Therefore, imaging was conducted from the intervertebral spaces, avoiding vertebral

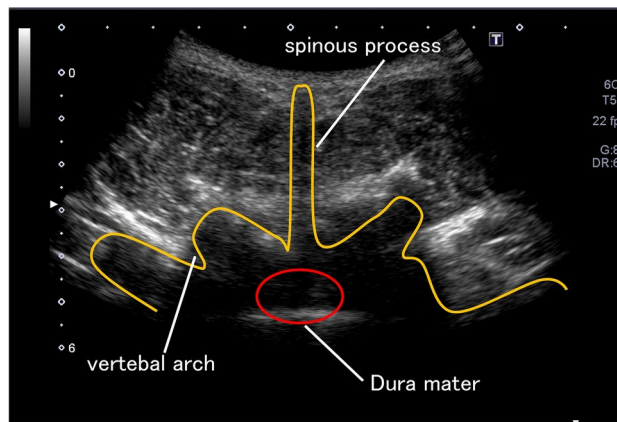


Fig. 7. Axial images of the lumbar spine and dural mater observed with ultrasound. L4-L5 dura mater.

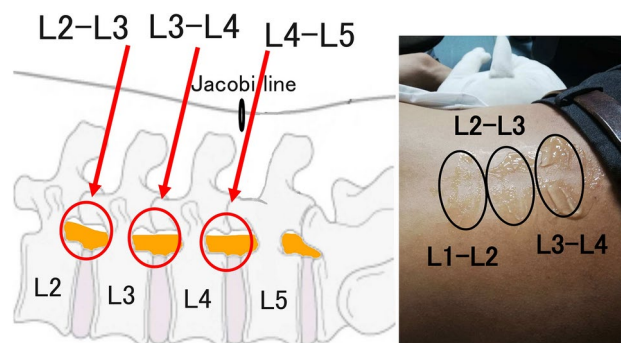


Fig. 8. Ultrasound imaging of the dura mater from between the spinous processes.

tissues as much as possible (Fig. 8). The locations targeted were the intervertebral spaces at the L2-L3, L3-L4, and L4-L5 levels of the lumbar spine to capture the pulsations of the dural mater. This selection was based on anatomical and clinical factors. The lumbar spine features an open intervertebral arch gap, which facilitates ultrasound evaluation. Additionally, the lumbar spine is a common site for conditions such as lumbar spinal canal stenosis in clinical practice. In contrast, the cervicothoracic level has a narrow intervertebral arch space, making it challenging to insert the ultrasound beam, and the presence of the spinal cord complicates the analysis of spinal fluid perfusion. The process for confirming vertebral levels is as follows:

1. By visualizing the long-axis image of the spinous processes on the caudal side of the Jacoby line at the midline, the L5/S1 spinous process is identified.
2. The probe is slid approximately 1–2 cm laterally to confirm the L5 lamina and the posterior surface of the sacrum.
3. Based on the L5 lamina and the posterior surface of the sacrum, the probe is moved to identify the lamina of each lumbar vertebral level.
4. After confirming the vertebral level, the dural sac pulsations are observed by imaging in the short axis through the intervertebral spaces.

To extract the pulsations of the dural mater from the captured videos as waveform data, speckle tracking was utilized. Speckle tracking, a technique that tracks unique interference patterns known as ‘speckles’ characteristic of ultrasound images, was implemented under the environment of Windows 10 using Python 3.7.3.

Specifically, we have clarified that the tracking was performed using OpenCV’s Lucas-Kanade method in Python 3.7.3 on Windows 10. The following Python libraries and versions were used in our analysis:

- Numpy 1.23.5
- Pandas 1.5.3
- OpenCV 4.7.0
- Statsmodels 0.10.2
- scikit-learn 1.2.1
- scipy 1.9.0

Furthermore, we have added details regarding the tracking settings used in our analysis, including:

- Kernel window size: User optional



Fig. 9. Measurement of electrocardiograms with limb guidance.

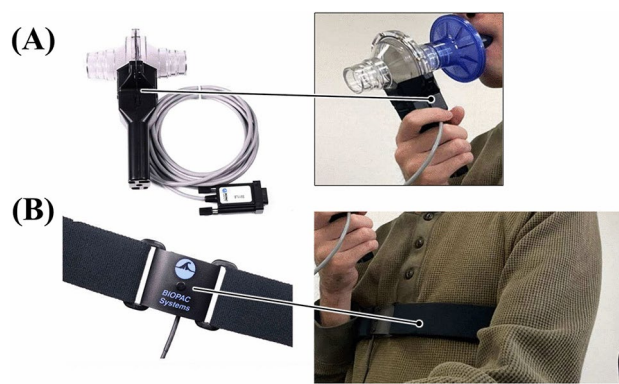


Fig. 10. Measurement of respiratory rate and respiratory movement. Measurement of respiratory volume by applying a pressure transducer to the mouth. A band transducer is placed around the chest to measure respiratory motion.

- Pyramid levels: Level3
- Number of iterations: 10
- Gaussian filter kernel size: 5×5

The captured video image was loaded and displayed on the screen, allowing the user to select the average speckle displacement of multiple points on the dura near the tissue of interest. The speckle displacement was then tracked, and the data was outputted as a CSV file. To minimize the effects of surface movements of body and hand tremors of the operator, the pulsations of the dural mater were obtained as relative displacements based on the tip of the spinous process as a reference point.

Heart rate and respiration were measured using the BIOPAC Student Lab system (BIOPAC Systems Inc., Goleta, California). This system consists of the MP36 unit and various transducers for physiological signal measurements. Electrocardiography was performed using the SS2LB transducer (BIOPAC Systems Inc., Goleta, California) with limb leads (Fig. 9). Respiration volume was measured using the pressure transducer SS11LB (BIOPAC Systems Inc., Goleta, California), while respiratory motion was measured using the Respiratory Effort Transducer SS5L (BIOPAC Systems Inc., Goleta, California) (Fig. 10). Additionally, respiration and heart rate measurements were conducted simultaneously with ultrasound imaging to compare with the pulsations of the dural mater.

Seasonal decomposition using STL

Time series data, when not subjected to smoothing or differencing processes, generally consist of three components:

1. Trend Component: Long-term, systematic variations that increase or decrease over time.
2. Seasonal Component: Variations that occur regularly, usually on an annual cycle or some other fixed cycle, exhibiting systematic changes with seasons. Even if not strictly on a yearly cycle, fixed variations repeated at the same intervals are also defined as seasonal components.
3. Residual Component: Components that do not fit into the above categories, such as noise, outliers, or sudden, singular changes.

Seasonal decomposition is a method used to remove the trend component and extract the seasonal component from time series data, capturing the characteristics of data with fixed periodicities like months or days. It finds wide application in fields such as economics and meteorology.

STL (Seasonal and Trend decomposition using LOESS : Locally Estimated Scatterplot Smoothing) is a seasonal decomposition technique that employs LOESS regression. It can capture local patterns even in the presence of anomalies or outliers, and it is robust to missing values. Additionally, it allows for the specification of the desired seasonal periods. Since it is not limited to monthly or daily frequencies, it can decompose time series data, such as dural pulsations, which do not adhere to specific dates, into trend and seasonal components as a pseudo-seasonal adjustment. In this study, we considered the heart rate and respiratory cycle as pseudo-seasonal cycles and performed STL to remove the trend component and extract the variations in the respiratory and heart rate cycles.

We have specified the software used for performing the STL analysis. The STL decomposition was conducted using statsmodels library in Python. Furthermore, we have added details regarding the tracking settings used in our analysis, including:

- **Kernel window size: 15 × 15**
- **Pyramid levels: Level3**
- **Number of iterations: 10**
- **Convergence condition: Movement less than 0.03**

The periods of respiration and heartbeats used as the reference for seasonal cycles were determined using the period detection feature built into the BioPAC system used for measurement. While the periods of respiration and heartbeats are not always constant and may fluctuate over time, for this study, we obtained the periods of all pulses within the measurement range and then used their average as the reference for the respiratory and heart rate cycles.

Granger causality test

Granger causality is a concept to determine the existence of causality in time-series data from the data alone. We say that there is a Granger causality from a time series variable X to a time series variable Y when the prediction of the value of data Y that changes with time can be better predicted based on the past values of Y and X than based only on the past values of Y itself. When a variable Y increases or decreases at the same time as a variable X increases or decreases, the prediction accuracy of Y is better if the increase or decrease of X is known when predicting Y, and vice versa. The method to determine this based on statistical hypothesis testing is called Granger causality test.

The following three statistical significance indicators are mentioned:

- p-value: A low p-value from the F-test (e.g., < 0.05) indicates that Y provides significant information for predicting X.
- Adjusted R²: Evaluates the improvement in model fit when adding past values of Y.
- Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC): These are used to compare model fit while considering model complexity.

For the Granger causality test, VAR models were created, including electrocardiogram (ECG), respiration motion (res_move), respiration flow volume (res_volume), dura mater, and seasonal components of the dura mater (STL with heartbeat cycle : seasonal_hb, STL with respiration cycle : seasonal_res).

Of the 36 VAR models created (6 subjects × 3 levels × 2 measurements), 33 showed stability. Table 1 shows a summary of the Granger causality estimation results, and these causal relationships are illustrated in Fig. 11. In the figure, the direction of the arrow lines indicates the direction of causality. At the same time, the thickness represents the strength of causality.

First, we focused on the causality between ECG and res_volume, res_move, and dura without considering STL. Despite the relationship between cerebrospinal fluid dynamics and heart rate and respiration being pointed out in previous studies, the current study did not provide Granger causality of causality between respiratory and cardiac cycles and dural pulsations. On the other hand, the causality between respiration movement (res_move) and respiratory volume (res_volume), which is anatomically evident, was established. Additionally, the

	res_volume→	res_move→	ECG→	Dura→	seasonal_res→	seasonal_hb→
→res_volume		23	3	0	0	0
→res_move	30		8	0	7	12
→ECG	5	1		0	16	17
→Dura	0	0	0		0	0
→seasonal_res	0	5	16	0		23
→seasonal_hb	0	4	30	0	28	

Table 1. Results of Granger causality estimation. Arrows indicate the direction of causality. Validation was performed on the 33 patterns that showed stability out of the VAR models created in the current study, recording the number of patterns in which causality was detected.

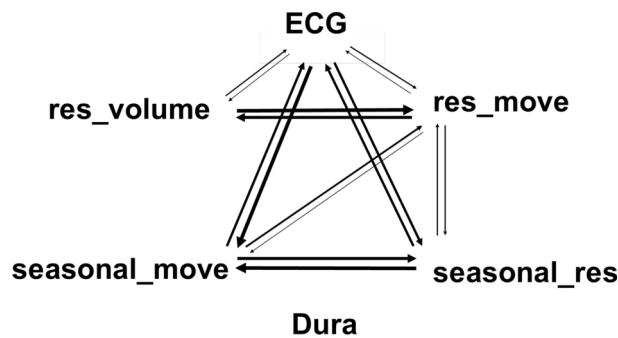


Fig. 11. Granger causality test for respiration, heart rate, and dura mater. The direction of the arrow lines indicates the direction of causality, while the thickness represents the strength of causality. Original waveform of dura mater : dura. Respiration movement : res_move. Respiration volume : res_volume. Heartbeat cycle seasonal component of dural canal isolated by STL : seasonal_hb. Respiratory cycle seasonal component of dural canal isolated by STL : seasonal_res.

causal relationship between respiration and heart rate, known as respiratory sinus arrhythmia (RSA), was also demonstrated.

Conclusion

The current study aimed to clarify the elusive properties of dural pulsation. We compared its characteristics to heart rate and respiration, noting that it exhibits $1/f$ fluctuations without consistent periodicity. We isolated respiratory and cardiac fluctuation components using STL, but initial Granger causality tests did not reveal a direct relationship between dural pulsation and these physiological processes. However, further analysis showed potential Granger causality post-decomposition, implying that dural pulsation might be influenced by both respiration and heart rate. Given the complexity indicated by the $1/f$ fluctuations, targeted analysis and a broader understanding of anatomy may be necessary for more conclusive insights.

Data availability

Data are available from the authors upon reasonable request.

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References

- Deyo, R. A., Mirza, S. K. & Martin, B. I. Back pain prevalence and visit rates: Estimates from U.S. national surveys, 2002. *Spine* **31**, 2724–2727 (2006).
- Covinsky, K. E., Lindquist, K., Dunlop, D. D. & Yelin, E. Pain, Functional Limitations, and Aging. *J. Am. Geriatr. Soc.* **57**, 1556–1561 (2009).
- Leveille, S. G. et al. Low back pain and disability in older women: Independent association with difficulty but not inability to perform daily activities. *J. Gerontol. Ser. A* **54**, M487–M493 (1999).
- Reid, M. C., Guo, Z., Towle, V. R., Kerns, R. D. & Concato, J. Pain-related disability among older male veterans receiving primary care. *J. Gerontol. Ser. A* **57**, M727–M732 (2002).
- Makris, U. E. et al. Restricting back pain and subsequent disability in activities of daily living among community-living older adults. *J. Aging Health* **30**, 1482–1494 (2018).
- Clinical Anatomy Of The Lumbar Spine, Second Edition. *eBay* <https://www.ebay.com/itm/364437550311>.
- Jokich, P. M., Rubin, J. M. & Dohrmann, G. J. Intraoperative ultrasonic evaluation of spinal cord motion. *J. Neurosurg.* <https://doi.org/10.3171/jns.1984.60.4.0707> (1984).
- Cushing, H. The third circulation and its channels. *Lancet* **209**, 851–857 (1927).
- Milhorat, T. H., Hammock, M. K., Fenstermacher, J. D., Rall, D. P. & Levin, V. A. Cerebrospinal fluid production by the choroid plexus and brain. *Science*. **173**(3994), 330–332 (1971).
- Orešković, D. & Klarica, M. The formation of cerebrospinal fluid: Nearly a hundred years of interpretations and misinterpretations. *Brain Res. Rev.* **64**, 241–262 (2010).
- Dreha-Kulaczewski, S. et al. Respiration and the watershed of spinal CSF flow in humans. *Sci. Rep.* **8**, 5594 (2018).
- Weed, L. H. Studies on cerebro-spinal fluid. No. III: The pathways of escape from the Subarachnoid Spaces with particular reference to the arachnoid Villi. *J. Med. Res.* **31**, 51–91 (1914).
- McComb, J. G., Davson, H., Hyman, S. & Weiss, M. H. Cerebrospinal fluid drainage as influenced by ventricular pressure in the rabbit. *J. Neurosurg.* <https://doi.org/10.3171/jns.1982.56.6.0790> (1982).
- Di Chiro G. New Radiographic and Isotopic Procedures in Neurological Diagnosis: Useful new diagnostic tools are a refinement of pneumoencephalography, a new tracer for radioactive brain scanning, and the use of radio-iodinated serum albumin injected into the cerebrospinal fluid cavities for head scanning purposes | JAMA | JAMA Network. <https://jamanetwork.com/journals/jama/article-abstract/1162973>.
- Yamada, S. Cerebrospinal fluid physiology: visualization of cerebrospinal fluid dynamics using the magnetic resonance imaging time-spatial inversion pulse method. *Croat. Med. J.* **55**, 337–346 (2014).
- Yamada, S. & Kelly, E. Cerebrospinal fluid dynamics and the pathophysiology of hydrocephalus: New concepts. *Semin. Ultrasound CT MRI* **37**, 84–91 (2016).
- Kimura, A. et al. Ultrasonographic quantification of spinal cord and dural pulsations during cervical laminoplasty in patients with compressive myelopathy. *Eur. Spine J.* **21**, 2450–2455 (2012).

18. Yamada, S. et al. Influence of respiration on cerebrospinal fluid movement using magnetic resonance spin labeling. *Fluids Barriers CNS* **10**, 36 (2013).
19. Lloyd, R. A. et al. Respiratory cerebrospinal fluid flow is driven by the thoracic and lumbar spinal pressures. *J. Physiol.* **598**, 5789–5805 (2020).
20. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation* **93**(5), 1043–1065 (1996).
21. Musha, T. Yamamoto, M. 1/f fluctuations in biological systems. In *Proceedings of the 19th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. Magnificent Milestones and Emerging Opportunities in Medical Engineering (Cat. No.97CH36136)* 6 2692–2697(1997).
22. Ivanov, PCh. et al. From 1/f noise to multifractal cascades in heartbeat dynamics. *Chaos Interdiscip. J. Nonlinear Sci.* **11**, 641–652 (2001).
23. Cleveland, R. B., Cleveland, W. S., McRae, J. E. & Terpenning, I. STL: A seasonal-trend decomposition procedure based on loess. *J. Offic. Stats.* **6**(1), 3–73 (1990).

Author contributions

RK and BK conducted data collection and data entry, performed the statistical analysis, and wrote the manuscript. Other authors, KI, YE, MN, YS, MI, ST, KO, ShOh, SM, TF, TK, SH, SeOh and SuOr contributed to the recruitment of subjects, collected their data, and approved the final manuscript. The authors declare that they have no competing interests. We did not receive grants or external funding in support of our research or preparation of this manuscript. We did not receive payments or other benefits or a commitment or agreement to provide such benefits from any commercial entities.

Declaration

All experimental protocols were approved by the institutional committee of Chiba University, and informed consent was obtained from all clinical subjects prior to conducting the experiments. Data are available from the authors upon reasonable request. The authors declare that they have no competing interests. We did not receive grants or external funding in support of our research or preparation of this manuscript. We did not receive payments or other benefits or a commitment or agreement to provide such benefits from any commercial entities.

Competing interests

The authors declare no competing interests.

Additional information

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