Intracranial pressure waves: characterization of a pulsation absorber with notch filter properties using systems analysis

Object. The relationship between the waveform of intracranial pressure (ICP) and arterial blood pressure can be quantitatively characterized using a newly developed technique in systems analysis, the time-varying transfer function. This technique considers the arterial blood pressure as an input signal composed of multiple frequencies represented in the output ICP according to the transfer function imposed by the intracranial system on the input signal. The transfer function can change with time and with physiological manipulations. The authors examined data obtained from canine experiments involving manipulations of ICP.

Methods. The authors analyzed 11 experiments from 3 normal mongrel dogs under conditions of normal ICP and with changes in ICP made by bolus injection, infusion, or withdrawal of cerebrospinal fluid by using time-varying transfer function.

Results. During normal ICP periods, the gain of the transfer function displayed a deep notch (≥1 log unit) centered at or near the cardiac frequency. In systems terms, the intracranial compartment under normal conditions appears to act as a notch filter attenuating the cardiac frequency input relative to other frequencies. Epochs of ICP elevation showed suppression of the notch, and the notch was restored when ICP returned to normal.

Conclusions. The intracranial system in these animals could be considered to include a pulsation absorber for which the target frequency appears to be close to the cardiac frequency. One possible source for such an absorber mechanism might be the free movement of cerebrospinal fluid, implying that impairment of this motion may have important clinical implications in various neurological conditions such as hydrocephalus. (DOI: 10.3171/PED/2008/2/7/083)

KEY WORDS • arterial blood pressure • hydrocephalus • intracranial pressure • pulsatility • pulsation absorber • transfer function analysis

Abbreviations used in this paper: ABP = arterial blood pressure; ARMA = autoregressive and moving-average; CSF = cerebrospinal fluid; FFT = fast Fourier transformation; ICP = intracranial pressure; OPS = optimal parameter search; TVTF = time-varying transfer function.

* Drs. Zou and Park contributed equally to this paper.
The past 2 decades have seen increasing interest in intracranial pulsatile phenomena, including the use of the ICP response to cardiac pulsations to characterize compliance. 

The ICP and ABP waves can be represented as a series of sinusoidal waves, consisting of the fundamental cardiac frequency and its multiple harmonics (discrete multiples of the cardiac frequency). A number of studies have used transfer function analysis to understand the relationship between the ICP and ABP. The transfer function may be thought of as reporting a gain, or ratio of amplitudes of the ICP to that of the ABP, and phase shift, calculated at each individual frequency, over the appropriate spectrum. The gain of the transfer function—a measure in the frequency domain describing how much of the ABP fluctuation is transmitted at a given frequency to the ICP—is calculated for these discrete frequency components. These techniques have limited ability to trace temporal changes in the system, which is afforded by newer time-frequency techniques.

Our study applies a newly developed TVTF technique. This technique was applied to carotid ABP input and ICP output recorded from anesthetized animals with and without artificial elevation of ICP. To anticipate the major finding of this paper, the gain of the transfer function illustrated sharp attenuation around the cardiac frequency during normal ICP epochs. In electrical engineering nomenclature, the attenuation of the gain at a specific frequency is a primary characteristic of a notch filter. A familiar example of a notch filter would be an electronic circuit that removes 60 Hz noise from electroencephalography or audio signals. From the physiological standpoint, the notch filter may serve the purpose of functional attenuation of a particular portion of the arterial pulsation as it is transferred into the vascular bed. To grasp the physiological meaning of this observed notch filter, we will discuss one possible physiological mechanism in the cranial system that could account for the notchlike features.

There is significant interest in whether perturbations to intracranial pulsations underlie the pathological condition of hydrocephalus and other varieties of increased ICP. Clinical studies have shown that the pulse amplitude of the ICP waveform can be used to predict treatment response in patients with hydrocephalus. Therefore, our findings may provide a computational perspective for understanding mechanisms underlying the link between pulsations and hydrocephalus and other pathophysiological conditions involving cerebral blood flow dynamics.

Methods

Experimental Procedures and Data Acquisition

The ABP and ICP were recorded during experiments performed in 3 adult mongrel dogs. All animals were treated humanely in compliance with the Guide for the Care and Use of Laboratory Animals, published by the US National Institutes of Health. The protocol for these experiments was approved by the Institutional Animal Care and Use Committee. Each animal was sedated, intubated, and anesthetized. After establishing carotid and femoral access by open surgical exposure, Microtip pressure transducers (Millar Instruments) were carefully placed in the right carotid artery and right femoral vein and in the parenchyma of the brain (using a bur hole in the right frontal bone). The catheters were secured by cannulating and suturing the vessel. Each pressure wave was continuously monitored and recorded using custom software (Labview, National Instruments); ABP and ICP recordings were taken synchronously. Data were digitized using a National Instruments data acquisition board with a sampling frequency of 33 Hz. Resting pressures were collected for at least 15 minutes before any ICP manipulations were attempted. Resting pressures were between 5 and 25 mm Hg, and over the course of the experiment ICP was elevated to 20–40 mm Hg above resting pressure. Intracranial pressure was manipulated by bolus injection (0.5–5 ml), infusions of saline (0.2–2 ml/minute), or withdrawals of CSF mostly via a catheter in the lower lumbar thecal space. At the conclusion of the experiments, the animals were humanely killed by anesthetic overdose.

Transfer Function Analysis

In earlier studies of system analysis applied to pressure pulse waves, transfer functions were calculated based on the FFT of input (ABP) and output (ICP) waveforms. Using spectral analysis, one fundamental frequency and multiple harmonic components are detected and transfer functions are evaluated at those discrete frequencies only. The gain at the fundamental frequency, for example, is calculated as the ratio of the amplitude of the fundamental spectral frequency (A_0/A_0). The gain at each of the harmonic components is estimated in the same way, but this method is not capable of depicting changes in the transfer function as the ICP changes (such as changes in the amplitude or shape of the waveforms) with time. To better understand the dynamics of the intracranial system, we have developed a new method, the TVTF, to enable us to trace and optimally visualize system changes resulting from the ICP changes over time. In Appendices A and B, we review the characteristics of the methods involved in the derivation of this new technique, which include ARMA model identification and transfer function from the ARMA identification technique. In the following section, we introduce TVTF derived from ARMA modeling that we used for the present study.

Time-Varying Transfer Function From ARMA Modeling

Transfer functions are mathematical representations of systems. Time-invariant transfer functions represent the gain and phase shift of any system as a function of frequency. The time varying technique allows the transfer function coefficients to be a function of the time and frequency (symbolically H [n, ω]). Therefore, the TVTF method is able to identify inherent nonstationary dynamics in biomedical systems. In this paper we introduce a straightforward approach to estimate TVTF. This approach is based on the concept of short-time Fourier transformation that breaks input and output data into small segments by using a sloping window. This sliding window segments the signal (or data) in the time domain. Then, transfer function analysis derived from ARMA modeling is performed to estimate the local frequency content for each segment. This approach is particularly suitable to analyze long experimental recordings and ideal for this particular study with recordings that exceed 15 minutes.

Figure 1 illustrates the procedure of computing TVTF.
which consists of several steps, including division of the input-output data set into short segments by simultaneously multiplying them with a window function. For example, the $k^{th}$ segment of input data $x(n)$ can be expressed as:

$$x_k(n) = x(n)w(n / M), 1 \leq k \leq K, 0 \leq n \leq M - 1$$  (1)

where $M$ is the length of each segment and $K$ represents the number of sliding segments. A rectangular window was used to segment data in the time domain:

$$w(n) = \begin{cases} 1 & \text{for } 0 \leq n \leq M - 1 \\ 0 & \text{otherwise} \end{cases}$$  (2)

The segments obtained by moving the window along the data were allowed to overlap (see Appendix D for details). For this study, $M = 2000$ data points (60.6 seconds with a sampling rate of 33 Hz) and 90% overlap ($\approx M$ step size), corresponding to 1800 data points that were used. Given a total $N$ of data points, the number of sliding segments $K$ can be generated by the following formula: $K = (N - M) / \text{step size}$. Each short segment can be considered a quasi-stationary segment. Subsequently, each segmented input–output data set is fitted by the ARMA model identification, with the model parameters identified using the OPS algorithm (see Appendix A). By splitting the data into short time segments, we are thus able to obtain many short-segment ARMA models, yielding locally time-invariant transfer functions, which characterize the system dynamics within each particular input–output segment. Finally, the set of transfer functions taken collectively indicates how the transfer function varies over time.

Data Analysis

The ABP and ICP data recorded from a total of 11 separate experimental sessions in 3 animals were retrospectively analyzed. These experiments consist of 4 sessions for Animal 1, 4 sessions for Animal 2, and 3 sessions for Animal 3. The duration of each session ranged from 6 to 30 minutes. A total of 11 data sets were visually examined and segment-ed into 2 different groups: resting epochs and epochs of ICP perturbation. A total of 24 segments were obtained and analyzed. Six of these fell within the resting period (either prior to manipulation or after manipulation was stopped and the ICP had returned to almost the same level as before the manipulation). The respiratory frequency component was removed by using the infinite impulse response digital filter (see Appendix E). Each data segment was normalized to 0 mean and unit variance before transfer function analysis was performed.

Results

Time-varying transfer function analysis revealed an unexpected notch in baseline recordings (the period before ICP manipulations began). A sharp and discrete minimum in the gain displayed as a deep notch ($\approx 1$ log unit) centered near the cardiac frequency was observed in all 6 resting segments (Fig. 2). In all cases in which ICP was disturbed, the notch was eliminated.

![Time-varying transfer function analysis](image)

**Fig. 1.** Diagram showing the procedure of computing TVTF. The gray box indicates a rectangular moving window. The transfer function (TF) is calculated in each window, which moves forward in time. The entirety of all transfer functions provides the TVTF in a time-frequency domain.
Presence of Notch in the Resting System

Typical ABP and ICP recordings at normal ICP levels are shown in Fig. 2A and B, respectively. The transfer functions were averaged over all sliding segments. The gain of the averaged transfer function shows a narrow notch at a frequency that appears to match the cardiac frequency (Fig. 2C left). The gain (in log units) at the frequencies below and above the cardiac frequency is around 0, indicating that the cardiac frequency-specific transfer is diminished. This is analogous to a notch filter. The phase angle as a function of frequency (Fig. 2C right) shows a sharp phase shift around the cardiac frequency, another well-known characteristic of notch filters. For 6 control periods for which a notch (≥1 log unit) was observed, the notch frequencies as a group were not statistically different from the heart rate frequencies observed during the same collection times (1.2 ± 0.2 Hz vs 1.0 ± 0.1 Hz, mean ± standard error of the mean), and the individual values of notch frequency differed from the heart rate frequency values by only 0.2 ± 0.1 Hz, for a mean relative error of 16% of cardiac frequency. Thus, the computed notch frequency was not identical in all cases to the heart rate, but it was significantly close compared with the dynamic range over which our values were measured (within a range from 0 to the Nyquist frequency 16.5 Hz). The recordings for the elevated ICP case are shown in Fig. 3A and B, and in this case neither the notch at the cardiac frequency (Fig. 3C left) nor the sharp phase jump (Fig. 3C right) is present.

A typical waveform of ABP and ICP recorded in normal and elevated ICP conditions is shown in the insets of Figs. 2 and 3. From visual inspection, the ICP waveform from an elevated ICP epoch clearly appears different from that of a normal ICP epoch (compare insets in Figs. 2B and 3B), and in fact looks quite similar to the arterial pressure (compare insets in Fig. 3A and B). Similar waveform patterns were obtained from other recordings. Morphological changes in the ICP waveform have been extensively reported under various physiological and pathological conditions. The features we observed are in agreement with previous reports.

Absence of the Notch in the Elevated ICP System

To examine the transient responses of the notch to an elevation of ICP, TVTF was calculated from the ABP and ICP recordings during artificial manipulation involving ICP changes. Figure 4A shows the data recorded during an experimental sudden increase in ICP.

Prior to the ICP increase, a notch in gain at the cardiac frequency range was present. The notch is visible and highlighted by yellow-green shown in 2D projection (Fig. 4B) and 3D view (Fig. 4C), indicating a sharp drop in gain of about 3 log units during this period. Immediately after the ICP was artificially elevated, however, the notch disappears, and it reappears as the ICP level returns to normal. The corresponding changes of phase angles are shown in Fig. 4D, in which the phase jumps from −180° to +180° in the vicinity of the cardiac frequency, but only while the ICP level is normal.

A similar analysis was applied to the ABP and ICP data recorded during a gradual increase in ICP (Fig. 5A). The color-coded map of TVTF demonstrates a transition from the presence of a deep notch to its disappearance during the increased ICP period (2D projection shown in Fig. 5B and 3D view shown in Fig. 5C). The results again suggest that the increase in ICP is responsible for the disappearance of the notch and of the phase jumps near the cardiac frequency (Fig. 5D).

Spectral Analysis in Presence and Absence of Notch

The traditional power spectrum of ABP and ICP data obtained from each experimental animal was computed during periods of normal ICP (when the notch was present) and elevated ICP (when the notch was absent). At the peak corresponding to cardiac frequency, the ICP shows a dramatic decrease in power (<50%) compared to ABP. At elevated ICP, with the notch absent, the two spectra were almost superimposable (Fig. 6). This finding is consistent with a change in the status of the notch in the different conditions.

Discussion

Systems identification, in the context of examining transfer functions of empirical data to determine how one signal may be derived from others, can yield mechanistic insights and new testable hypotheses. In this study, we observed a
Intracranial pulsation absorber

**Fig. 4.** Graphs showing the disturbance of the notch caused by an abrupt increase of ICP. A: The ABP (upper) and ICP (lower) recordings. B and C: A color-scaled gain of the TVTF projected in the time and frequency domain (B) and the 3D color-scaled TVTF, which consists of time, frequency, and gain (C). The yellow-green color indicates a deeper notch. A short segment of the observed notch disappears as the level of ICP increases and reappears as the level returns to the resting state. D: A 3D color-scaled TVTF that consists of time, frequency, and phase angle. A segment in which a mixture of red and blue is present indicates a sharp phase jump. This sharp phase jump disappears as the ICP level increases and reappears as the level returns to normal.

**Fig. 5.** Graphs showing the disturbance of the notch caused by a gradual increase of ICP. A: The ABP (upper) and ICP (lower) recordings. B and C: A color-scaled gain of the TVTF projected in the time and frequency domain (B) and the 3D color-scaled TVTF that consists of time, frequency, and gain (C). The yellow-green color indicates a deeper notch. Notches shown to be quite complex disappear after the ICP level starts to increase and remains high. D: A 3D color-scaled TVTF that consists of time, frequency, and phase. A segment in which a mixture of red and blue is present indicates a sharp phase jump. The sharp jumps in phase seen at a lower ICP disappear as the ICP level increases.
previously unreported property of the relationship of the arterial blood pressure waveform and the intracranial pressure waveform: a marked drop, or notch, in the efficiency with which the ABP pulse is transmitted into the cranium (as measured by the ICP) at the cardiac frequency, during normal resting ICP periods, and that this marked drop is eliminated during periods of elevated ICP.

Detection of the Notch

Other investigators have used transfer function analysis of ICP waveforms. Why has this notch phenomena not been previously reported? The reason is that only several frequencies (fundamental and first several harmonic frequencies) were used to represent and simplify the estimated transfer function, given the fact that most of the signal power is concentrated at the fundamental and its harmonics. The sparse points of transfer function, however, cannot capture the detailed structure of such a narrow notch.

The TVTF derived from ARMA modeling introduced in this study reveals a notch that appears centered around a frequency corresponding to the heartbeat under normal ICP conditions. This technique highlights the shape of the gain of the transfer function at or near cardiac frequency and also provides a more efficient way to observe its dynamics in response to changes in physiological conditions. The phase of the transfer function also varies as frequency changes. Under normal ICP conditions, a sharp phase shift around the cardiac frequency was observed. Under elevated ICP conditions, the gain significantly increased (the notch disappeared) and the sharp phase shift present under normal ICP conditions was not observed. This is consistent with earlier observations in other high ICP conditions—such as hypertension and hypercapnia in animal experiments—and hypertension in human patients—such that transfer functions became flatter with higher ICP caused by artificial disturbances or pathological conditions. The new computational techniques make the notch easier to see and study,

Fig. 6. Graphs showing the power spectral densities obtained from ABP (dotted lines) and ICP (solid lines) at normal ICP (A–C) and elevated ICP (D–F) for 3 animals.
allowing future application to animal models of pathophysiological conditions and human clinical data. The effectiveness of algorithms of TVTF involved in the study has been confirmed by both simulation signals and real signals (2,48,50) (see Appendix F).

Notch Filter and its Disappearance

In the resting state for all 3 animals, the gain showed a sharp minimum (a large attenuation of gain) around the cardiac frequency, which we have called a notch filter. This notch was observed in all 6 resting episodes. Infusion of artificial CSF had the effect of transiently eliminating the notch. This notch disappeared with infusion of CSF that changed the level of ICP, suggesting that in this system a presence of the notch is “normal” and its absence is “abnormal.” The presence of the notch around the cardiac frequency implies the existence of a mechanism for specifically attenuating the main pulsatile component of the arterial pressure waves entering the brain. It is possible that the episodes analyzed as resting epochs lacking the notch were contaminated by unknown details of the experiment or unspecified physiological conditions.

Possible Origin of The Notch Filter

It is impossible from these data sets to determine the precise underpinnings of a notch, but it may be useful to propose a biomechanically plausible mechanism. An anatomical origin for a notch filter, limiting the amplitude of the pulsations in flow at the cardiac frequency, could arise from the structural relationship of the cerebral vasculature to the CSF spaces. Schematic diagrams of the cerebral vasculature during hypothetical nonpulsatile flow, then during realistic systole and diastole states, are shown in Fig. 7A–C, respectively.13 The relationship between elastic arteries and the venous system in a closed cranial cavity was initially diagrammed by Davson,13 and the adapted versions of the diagram are shown in Fig. 7D–F, which correspond to Fig. 7A–C, respectively. Viewing the movement of CSF as a mass linking enlargement of the elastic arterial vessels during systole to the compression of veins separated by some distance and the rebound narrowing of arterial vessels during diastole (Fig. 7) as a mass-spring-dashpot mechanical system, result in a model with a characteristic frequency governed by second-order differential equations. Such a mechanical model,15 or its analogue second-order circuit (Fig. 8A) would yield behavior of a notch filter.

Notch filters are well known in engineering, but less known in biology and medicine. Analogies with other systems that display notch filter properties can inform us where to look to determine how such a system could be adjusted to a particular frequency and what aspects of the system could be altered to make the notch disappear. For example, in the simple electrical circuit model (Fig. 8A), the parameters that determine characteristics of the system such as notch frequency and the sharpness of the notch (called “Quality” in circuits) include inductance (L) and capacitance (C). The notch frequency (or center frequency) is given by \( f = \frac{1}{2\pi \sqrt{LC}} \). The sharpness of the RLC series notch filter can be described by \( \frac{1}{2\pi f R} \). Figure 8B shows various notches at different center frequencies, which were generated by 4 different combinations of these parameters (see Appendix G for the derivation of gain and phase angle), and Fig. 8C shows mechanical equivalents of the electrical system. The characteristics of the notch filter can thus be interpreted in physiological terms: the resistor (R) is analogous to the input resistance to arterial blood flow, the inductor (L) is analogous to the mass of CSF, the capacitor (C) is analogous to fluid volume storage (this also includes vessel wall elas-
ticity) involved, and the additional resistor (Rc) is analogous to the resistance to capillary blood flow (compare Figs. 7A and 8C). In the present data, the characteristic oscillatory mode in the intracranial system, leading to the attenuation of intracranial pulsations, appears specifically adjusted to the input ABP.

Because we are involving living tissue rather than a simple, fixed circuit, these parameters may change with time or physiological state. In particular, they may change with changes in heart rate, ICP, and other physiological variables; our data demonstrate changes with ICP manipulations explicitly. How these parameters would change with normal variations in heart rate, tissue injury, hydrocephalus, and other variables will be the basis for further studies.

**Purpose of the Notch Filter in Cerebral Physiology**

This notch at the cardiac frequency may represent the first direct demonstration of the existence of a pulsation absorber inside the cranium. Particularly, the importance of intracranial pulsations near the cardiac frequency has been addressed from theoretical model studies proposed by Egnor and colleagues. Unlike soft organs, the brain is surrounded by a rigid skull and requires a watery cushion such as CSF to compensate and attenuate the strong pulsations generated by arterial pressure waves entering the cranium. One of the benefits of this attenuation mechanism might be the ability to protect the delicate cerebral microcirculation and capillaries.

Considering that the variations in the precapillary arteriolar pressure are probably larger than the variations in the postcapillary venous pressure, variations in the mean capillary pressure (which would likely represent our measured ICP waves) would reflect variations in the arteriovenous pressure gradient, and hence flow, in the microvasculature. Under such conditions a system that buffers the ICP pulsation amplitude would also be expected to buffer the variations in the flow and wall shear in the microvascular beds. If the cerebral microvasculature performs better with smaller amplitudes of pressure (wall strain) or flow (wall shear), a pulsation absorber would have significant value, and its disruption could have important pathophysiological consequences. Similar effects have been demonstrated in cerebral and other microcirculatory beds.

This approach can offer a new way to consider intracranial compliance, which from the neurosurgical perspective has been typically based on the frequency-independent derivative of pressure (P) with respect to volume (V), or dP/dV. This study suggests that intracranial compliance may be frequency dependent. The realization that there may be a particular mechanism by which systems handle inputs of different frequencies differently suggests new ways to study the pathogenesis of hydrocephalus and other ICP-related conditions. Normal pressure hydrocephalus, slit ventricle syndrome, and compensated hydrocephalus would be candidates for study using systems identification techniques, especially as noninvasive imaging technology permits more widespread data gathering. Valid next steps would include characterization of changes in the notch filter mechanism of experimental animals with the onset of hydrocephalus and response to shunting and the exploration of pressure waveforms in humans to study the equivalent transfer functions in clinical situations. The significance of the systems analysis approach can be evaluated by answering

---

**Fig. 8.** Diagram of an electrical circuit analogy (RLC notch filter). A: A simple RLC (resistor [R], inductor [L], and capacitor [C]) series notch filter circuit diagram. B: Graph of a notch filter frequency response. Depending on the combination of the parameter values, the center frequency and the width of the notch filter can be varied. Three different gain curves (top panel) and corresponding phase curves (bottom panel) were obtained with 3 combinations of the parameter values: (R = 50[Ω], L = 25[mH], C = 400[pF]); (R = 50, L = 480, C = 40); and (R = 40, L = 700, C = 10). To compare the relative values, each parameter value was normalized by the maximum value, and the following sets were obtained: (R = 1, L = 0.04, C = 1); (R = 1, L = 0.7, C = 0.1); and (R = 0.8, L = 1, C = 0.025). The notch frequency (or center frequency) is determined by $1/\sqrt{LC}$ (gray arrow in the middle of the gain curve), and consequently the notch frequency will remain at 1 particular frequency as long as the product of L and C remains fixed. The bottom panel in B shows a sharp phase shift around the notch frequency. C: Diagram of an extension of the simple notch filter shown in panel A and the mechanical analogy.
Intracranial pulsation absorber

the question: are there aspects of the system that can be explainable when the frequency response of the system is considered, rather than limiting analysis to the steady state? Ultimately, the importance to neurosurgery of the focus on frequencies and pulsations will be evaluated on the strength of the diagnostic and therapeutic implications that emerge.

As a result of these observations, several important experiments are suggested for further research with this tool: 1) generalization to the unanesthetized state and other species, particularly humans, is critical to any clinical implication; 2) the dynamics of how the notch frequency might vary with cardiac frequency and whether errors of “frequency tuning” play any role in pathophysiology need to be studied; and 3) regarding the proposed attenuation of the pulsatility of capillary flow, testing by direct observation would be more powerful than indirect study through transfer functions. Velocity of motion in microvessels in the brain with an intact cranium is a theoretically measurable quantity (though practically this is very difficult). The “pulsation absorber” concept could be directly tested if and when these measurements are available.

Limitations of This Study

Our analysis of the data, using the ARMA model, indicates 2 main features: 1) that there exists a sharp notch in the frequency spectrum of the arterial-to-ICP transfer function indicating that the cranium is effective in suppressing particular frequencies of the arterial input from entering the cranium, and 2) that the location of this notch filter is close to the heart rate of the animal. Other work investigating high-frequency components of the transfer function also showed mitigation of the cardiac frequency and its harmonics, but with a much broader notch feature than indicated by the ARMA model. One limitation of our work is intrinsic in the physiology of the animal. Respiration causes significant variation in ICP but only limited variation in ABP. Thus, the low frequency portion of the transfer function is altered by respiration. We have attempted to mitigate the effects of respiration on the transfer function by using filters to eliminate these components, but it is possible that these filters modify the transfer function from its real form. As an example, in a number of data sets we have removed this respiratory filter and found that the sharpness of the notch is significantly dulled. Future experiments will explore the effect of respiration on the transfer function and its influence on the sharpness of the notch. Finally, our data were collected in dogs with a normal heart rate, and thus the greater part of the spectral power exists only in the cardiac frequency and its harmonics. This type of arterial input spectrum may also modify the measured transfer function to favor the cardiac fundamental frequency over other frequencies, thus giving the notch a sharper appearance. This effect can be investigated by randomly pacing the animal, for example, and will also be the subject of future investigations.

Clinical Implications and Future Directions

Possible implications that this work may have for clinical neurosurgery are, of course, speculative. With that caveat, clinical conditions that might be expected to perturb the ability of freely flowing CSF to cushion the effect of pulsatile input might have an impact on the brain by means of a change in the waveform of blood flow in small vessels.

Pathological entities that would interfere with these processes would include intra- or extraventricular obstructive lesions (aqueductal stenosis, cysts, Chiari malformations) as well as changes in vessel elastance (as in postinflammatory or posthemorrhagic arachnoid thickening or vasospasm). Thus many of the factors generally considered to contribute to the development of hydrocephalus may yield to study by techniques focusing on the waveforms of pressure or flow. Particular insights may come in previously counterintuitive situations such as slit ventricle syndrome and apparently compensated ventriculomegaly, in which optimal therapy remains controversial and problematic.

Conclusions

The results of this study have demonstrated that: 1) a pulsation absorption mechanism appears as a notch filter under normal physiological conditions and in particular leads to attenuation around the primary cardiac rhythm frequency; 2) this notch disappears when the ICP level is increased, indicating that the frequency-specific attenuation of the cardiac frequency input is lost; and 3) the notch returns from high to normal. This new technique, the TVTF, is a powerful tool for examining physiological dynamics.

Disclosure

Financial support for this study was provided by The Webster Family and the NJIT-HMS Initiative on Hydrocephalus to Rui Zou, Ph.D., Eun-Hyong Park, Ph.D., and Joseph R. Madsen, M.D., and by the BrainChild Foundation to Erin McCormack Kelly, Ph.D., Michael Egnor, M.D., and Mark E. Wagshul, Ph.D.

Acknowledgments

Drs. Rui Zou and Eun-Hyong Park contributed equally to this paper. We thank Laurel Fleming for copyediting the manuscript. We express our gratitude to James P. (Pat) McAllister, Ph.D., Marion L. (Jack) Walker, M.D., and Curt Stewart for their helpful review and strong support of this work.

Appendices

Appendix A: ARMA Identification

Autoregressive and moving-average modeling is a parametric method used to model input and output signals from physiological systems. As mentioned previously, in the intracranial system, input and output signals are the ABP measured in the carotid artery and the ICP measured in the parenchyma, respectively. An ARMA model can be written as:

\[
y(n) = \sum_{i=1}^{p} a_i y(n-i) + \sum_{j=0}^{q} b_j x(n-j) + e(n) \tag{A1}
\]

where \(x(n)\) and \(y(n)\) represent input and output signals, respectively. The variable \(e(n)\) is the prediction error. Variables \(p\) and \(q\) are model order, and \(a_i\) and \(b_j\) are model parameters. In the stationary case, model parameters are constant, whereas in the nonstationary case, model parameters are changing with time, that is, \(a_i(n)\) and \(b_j(n)\).

System identification of an ARMA model consists of determining the model order and model parameters from input–output data. The estimation of model parameters relies on correct model order selection. Some algorithms are available to identify stationary and nonstationary ARMA models, such as the conventional Akaike’s information criterion and minimum description length for determining the approximate maximum model order, and recursive least-square and least-mean-square for parameter identification. Most recent algo-
rithms of fast orthogonal search,31 OPS,32 and time-varying OPS30 have been shown to be more robust than conventional identification algorithms. This robustness is due to their accurate model order selection criteria and resultant accurate parameter estimation. For the present study, the algorithm of OPS developed by Lu et al.32 was chosen to identify the ARMA model because of its proven ability to accurately and effectively identify significant model terms compared with other available algorithms (see details in Lu et al., 200130).

Appendix B: Transfer Function From ARMA Identification

Transfer function measurements represent the key description of the linear dynamic relationship between the input and the output. In the present study, transfer function physically corresponds to pressure transmissibility from the arterial tree to the intracranial parenchyma. Time-invariant transfer function, as a function of frequency, H(ω), can be derived from a time-invariant ARMA model and is described as follows:

\[ H(\omega) = \sum_{k=1}^{q} b_k \exp(-j\omega k) \]

\[ 1 + \sum_{k=1}^{p} a_k \exp(-j\omega k) \]

The magnitude of H(ω), |H(ω)|, represents the system gain and is the ratio of output (ICP) to input amplitude (ABP) at each frequency. The phase angle of H(ω), θ(ω), describes the timing of output relative to the timing of input at each frequency. A positive phase indicates that output leads input, whereas a negative phase means that output lags input.

In contrast to the classical FFT-based method (see Appendix C) in which the spectral resolution is limited by available data length, the spectral resolution of transfer function calculated from ARMA modeling is not dependent on data length. This is a result of the fact that the ARMA model produces an accurate model of the data that is not constrained to the same time frame as the actual data, and can be made stationary with increased spectral resolution. Therefore, compared with classical nonparametric FFT-based methods, the parametric approach enhances spectral resolution and improves performance with shorter data records, making it easier to satisfy stationary requirements.

Appendix C: Transfer Function Obtained From the FFT Method

The transfer function based on the conventional nonparametric FFT, H(ω), is the ratio of the cross-spectrum of the input and output (Pxy(ω)) to the auto-spectrum of the input (Pxx(ω)):

\[ H(\omega) = \frac{P_{xy}(\omega)}{P_{xx}(\omega)} \]

The periodogram is generally used to calculate the power spectrum, which can be described as

\[ P(\omega) = \frac{1}{NT} \left| \sum_{n=0}^{N-1} x(n)w(n)e^{-j\omega n} \right|^2 \]

where w(n) is the window function and T is the data sampling interval. This method assumes that the signal is stationary (the morphology of the oscillations does not change with time). Unfortunately, most biological signals fail to satisfy these 2 criteria, and this is a classic limitation of FFT-based methods. Transfer function analysis was repeated with the same data segment shown in Figs. 2 and 3, but with the FFT-based method. A notch was observed when the ICP level was normal (Fig. 9 upper) and it was eradicated when the ICP level was elevated (Fig. 9 lower). The FFT-based method provides a consistent result except for the fact that ARMA modeling produces smoother curves than those obtained from the FFT-based method.

Appendix D: Window Length, Step Size, and Window Function

Window length must be determined empirically. The length should not be too short due to the impact on frequency resolution, and conversely it should not be too long so that “nonstationarity” of the data set can be avoided. In this analysis, we chose 2000 points that were optimized with trial and error. The purpose of using a moving window with 90% overlap (which is equal to a 10% step size) is to smoothen and reduce large fluctuations of the estimation, which occur due to the random nature of signals under investigation. This “windowing” technique is quite commonly used in spectral analysis. As for the step size, it controls the portion of the data included in the average process. As the step size decreases, more portions of the data are overlapped, and those overlapped portions are redundantly averaged. The number of frames (the number of moving windows) increases. For our analysis, we used a rectangular shape for the window. Generally, the distortion caused by multiplying a window function with a time sequence results in “smearing of the spectrum,” and in that case, narrow spectral peaks cannot be distinguished from each other. In the present study, however, we mainly considered the cardiac frequency, a single frequency component. Thus, exploring the different window function versus using the simple rectangular window is a choice rather than a requirement, improving, to some degree, the quality of estimation.

Appendix E: Filters Used for Removing Respiratory Cycle

For the approach of preprocessing to eliminate respiration frequencies, which is approximately between 0.15 and 0.3 Hz, we used a Chebyshev Type II IIR filter (“cheby2ord” and “cheby2” in Matlab, The MathWorks, Inc.) to block respiration frequency. The parameters used are the following: pass-band corner frequency (0.01/Hz, 0.5/Hz), stop-band corner frequency (0.1/Hz, 0.35/Hz) with pass-band ripple at 0.1dB (no more than 0.1dB losses in the pass-band), and stop-band attenuation at 10dB (at least 10dB attenuation in the stop-
Intracranial pulsation absorber

band), in which “nt” indicates normalized frequency defined as the sampling frequency divided by 2. Other approaches used in preprocessing, such as the IIR notch filter (“iirnotch” in Matlab) and low-pass filtering produced no change in the notch being detected around the cardiac frequency. In the IIR filter, the relationship between phase and frequency are nonlinear. This phase distortion was eliminated by using “filtfilt,” which is the “zero-phase digital filtering” function in Matlab.

Appendix F: Technical Advantages

The validity that includes accuracy, reproducibility, and applicability of the techniques used in this study has been proven by many successful biomedical applications.\textsuperscript{2,6–36} The technical advantage of TVTF derived from ARMA modeling introduced in the study is 3-fold: 1) a parametric method to derive the transfer function from ARMA, which allows characterization of system dynamics with only a few parameters; 2) the OPS algorithm ensures an accurate estimation of transfer function, with estimated ICPs following the measured data well and prediction error consistently low (Fig. 10); and 3) with the sliding window approach a 3D TVTF (consisting of time, frequency, and gain [or phase]) can be used to visualize the dynamic response of the intracranial system to changes in mean ICP.

Appendix G: Gain of RLC Series Notch Filter Circuit Transfer Function

A time domain signal can be transformed into the complex s-domain consisting of two variables ($s = \sigma + j\omega$: exponentially changing amplitude governed by real value $\sigma$ and frequency $\omega$) through the Laplace transformation. Since s-domain representation of the voltage across a resistor, an inductor, and a capacitor can be represented as $R$, $sL$, and $1/sC$, respectively, the transfer function (defined as output voltage divided by input voltage) can be written as ($sL + 1/sC)/(R + sL + 1/sC$; see the circuit diagram in Fig. 8A).\textsuperscript{27,43} Therefore, for the RLC notch filter, transfer function can be obtained as:

$$H(s) = \frac{(s^2 + \frac{1}{LC})}{(s^2 + \frac{R}{L}\cdot s + \frac{1}{LC})} \quad \text{(G1)}$$

By taking the only complex part ($s = j\omega$), the system’s frequency response can be obtained as follows:

$$H(j\omega) = \frac{(j\omega)^2 + \frac{1}{LC}}{\left((j\omega)^2 + \frac{R}{L}\cdot j\omega + \frac{1}{LC}\right) = \frac{1}{LC} - \omega^2} \quad \text{(G2)}$$

Let

$$A = \left(\frac{1}{LC} - \omega^2\right) \text{ and } B = \left(\frac{R}{L}\omega\right)$$

Then, the equation (G2) can be written as follows:

$$H(j\omega) = \frac{A}{A + iB} = \left(\frac{A^2}{A^2 + B^2}\right) - i\left(\frac{A\cdot B}{A^2 + B^2}\right) = a + i\cdot(-b)$$

where

$$a = \frac{A^2}{A^2 + B^2} \text{ and } b = \frac{A\cdot B}{A^2 + B^2}$$

The magnitude of the complex variable yields

$$\frac{1}{\sqrt{(\frac{1}{LC} - \omega^2)^2 + (\frac{R}{L}\omega)^2}} \quad \text{(G3)}$$

The amplitude plot shown in Fig. 8B can be obtained by taking the absolute value of the magnitude in (G3):

$$\text{Gain (or amplitude)} = \left|\frac{1}{\sqrt{(\frac{1}{LC} - \omega^2)^2 + (\frac{R}{L}\omega)^2}}\right| \quad \text{(G4)}$$

The phase angle can be described by the trigonometric function (arctangent function) of complex variables:

$$\text{Phase angle} = \tan^{-1}\left(-\frac{b}{a}\right) = \tan^{-1}\left(-\frac{B}{A}\right) = \tan^{-1}\left(-\frac{\frac{R}{L}\omega}{\frac{1}{LC} - \omega^2}\right) \quad \text{(G5)}$$

References

34. O’Rourke MF, Safar ME: Relationship between aortic stiffening and cerebrovascular disease in brain and kidney: cause and logic of therapy. Hypertension 46:200–204, 2005

Manuscript submitted November 21, 2007. Accepted April 4, 2008.
Current address for Dr. Kelly: Magnetic Resonance Division, Toshiba America Medical Systems, Inc., Tustin, California.
Address correspondence to: Joseph R. Madsen, M.D., Department of Neurosurgery, Children’s Hospital Boston, Harvard Medical School, Hunnewell 244, 300 Longwood Avenue, Boston, Massachusetts 02115. email: joseph.madsen@childrens.harvard.edu.