What is the ultimate goal in neural regulation of cardiovascular function?

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Prakash, E. S., Madanmohan, and Gopal Krushna Pal. What is the ultimate goal in neural regulation of cardiovascular function? Adv Physiol Educ 28: 100–101, 2004; 10.1152/advan.00013.2004.—We used the following multiple-choice question after a series of lectures in cardiovascular physiology in the first year of an undergraduate medical curriculum (n = 66) to assess whether students had understood the neural regulation of cardiovascular function. In health, neural cardiovascular mechanisms are geared toward maintaining (A) cardiac output, (B) total peripheral resistance (TPR), (C) arterial blood pressure (BP), (D) tissue blood flow. The same question was administered to 275 graduates preparing for postgraduate exams (but not following the same series of lectures as the undergraduates). In both groups, we found a large proportion of incorrect answers (70% in undergraduates and 85% in graduates) and sorted this out by offering a step-by-step explanation and two examples and found it successful. 1) What happens to BP and heart rate (HR) when a person loses 500 ml of blood (~10% of blood volume) in one minute? 2) What happens to your BP and HR as you get out of bed after a night’s sleep? Flow = perfusion pressure/resistance to flow; cardiac output = BP/TPR; BP = cardiac output × TPR = [stroke volume (SV) × HR] × TPR. In both examples, BP decreases and is rapidly brought into the normal range by the arterial baroreflex mechanism. TBF is regulated chiefly by varying local vascular resistance (autoregulation). In summary, the ultimate goal of all neural cardiovascular reflex mechanisms is to maintain arterial BP within a range in which tissues can regulate their own blood flows. Cardiovascular control during exercise was used as an example to emphasize these facts. A discussion of this kind triggered interest in the minds of students and graduates, helping them get rid of a major misconception in about 20–40 minutes.

Table 1. Distribution of answers from among options provided

<table>
<thead>
<tr>
<th>Level</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undergraduates</td>
<td>30</td>
<td>14</td>
<td>23</td>
<td>33</td>
</tr>
<tr>
<td>Graduates</td>
<td>41</td>
<td>2</td>
<td>12</td>
<td>45</td>
</tr>
</tbody>
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Values are expressed as percentage.

We have sorted out this problem by offering a step-by-step explanation and a couple of examples and found it successful. The explanation goes like this. It is important to keep in mind the relation between the first three options. First of all,

\[ \text{flow} = \text{perfusion pressure/resistance to flow} \]  
\[ \text{cardiac output} = \frac{\text{BP}}{\text{TPR}} \]  
\[ \text{Alternatively,} \]  
\[ \text{BP} = \text{cardiac output} \times \text{TPR} \]

Also,

\[ \text{BP} = \text{stroke volume (SV)} \times \text{heart rate (HR)} \times \text{TPR} \]

Consider the following two examples:
1) What happens to BP and HR when a person loses 500 ml of blood (~10% of his blood volume) in one minute?
2) What happens to your BP and HR as you get out of bed after a night’s sleep?

In both examples, venous return decreases. As a result, SV and cardiac output decrease, and BP falls. The fall in BP is detected by arterial baroreceptors, and the response consists of an immediate increase in HR followed by an increase in TPR. This is the arterial baroreflex mechanism, which serves to rapidly control and maintain arterial BP within the normal range (1). If BP is normalized, then “neural cardiovascular reflex mechanisms” have attained their goal. The arterial baroreflex mechanism is an important mechanism that serves to maintain BP. Different mechanisms are activated depending on the prevailing BP, but all of them serve to bring it into the normal range. One may summarize mechanisms that cause changes to BP and physiological defense mechanisms as in Table 2.

It is clear that, in each case cited above, the ultimate goal is to maintain BP that is equal to the product of SV, HR, and TPR.
blood flow (here TBF) =

\[
\frac{\text{perfusion pressure (here BP)}}{\text{resistance to flow (here resistance of local vascular bed)}}
\]  

When BP changes, all tissues, including the brain, kidneys, heart, skeletal muscle, and viscera, are able to maintain their blood flows within a range dictated by their metabolic requirements. This phenomenon, called autoregulation, is mediated by changes in local vascular resistance (2). For example, the brain is capable of autoregulating its flow when the mean arterial pressure is between 65 and 140 mmHg (3). The following points need to be clearly noted. By definition, autoregulation is independent of neural innervation. Local vascular resistance is the resistance to blood flow in a particular tissue. It should not be confused with TPR, a value that is calculated when BP and cardiac output are known.

In summary, the ultimate goal of all neural cardiovascular reflex mechanisms is to maintain arterial BP within a range in which tissues can regulate their own blood flows. It follows that, when BP is outside of this normal range, tissues decline in their ability to autoregulate their flows with predictable consequences. It is the pressure gradient in circulation that drives flow, and it is the maintenance of BP within limits appropriate for the prevailing physiological state—sleep, standing, dynamic exercise, to mention a few—that is important.

After finishing with this explanation, we ask our students whether there is an exception to this paradigm of neurocardiovascular control. For example, during exercise, the metabolic rate increases depending on work intensity, and the demand for O₂ and energy substrates increases. Because oxygen delivery to tissue equals cardiac output times arterial blood oxygen content, increasing cardiac output is the most important mechanism for increasing O₂ delivery. The increase in sympathetic activity during exercise causes an increase in HR, SV, and vascular resistance in inactive skeletal muscle and viscera (4). As a result, BP increases. However, an increase in BP at this time does not lead to as much baroreflex-mediated lowering of HR and TPR as occurs at rest, because the arterial baroreflex mechanism regulating HR and vascular resistance is reset (i.e., its gain or effectiveness is reduced); therefore, cardiac output, vascular resistance in inactive tissue, and BP increase. This serves to deliver more O₂ and energy substrates to actively metabolizing tissue. Looking back at \( \text{Eq. 1} \), it is clear that increasing BP as well as reducing local vascular resistance can meet a demand for increased blood flow. However, changing local vascular resistance (i.e., autoregulation) is quantitatively much more important, because small changes in vessel diameter produce large changes in blood flow. It must be noted, however, that, despite large increases in cardiac output, mean arterial pressure does not normally increase beyond a limit (e.g., 140 mmHg), even during severe exercise. This is because significant increases in cardiac output, as occurs during intense dynamic exercise, is accompanied by significant decreases in TPR due to accumulation of vasodilator metabolites in actively exercising skeletal muscle (4). The large drop in TPR (and therefore BP) elicits a baroreflex-mediated increase in HR and vascular resistance in inactive tissue. Thus, although the arterial baroreflex mechanism is reset during exercise, it still functions to prevent BP from either falling below or rising above a certain range as the case may be.

In conclusion, it is clear that, in any physiological state, mechanisms impose restrictions on values that BP can take by varying cardiac output and TPR. That is the be-all and end-all of neural cardiovascular regulatory mechanisms. A discussion of this kind triggered interest in the minds of our undergraduate students and graduates, helping them get rid of a major misconception, and made their analysis of cardiovascular regulation systematic, logical, and rewarding. And it took us only about 20 minutes to do this with the undergraduate students and 40 minutes with the graduates.

REFERENCES


### Table 2. Mechanisms causing changes to BP and physiological defense mechanisms

<table>
<thead>
<tr>
<th>Primary Change</th>
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</thead>
<tbody>
<tr>
<td>Decrease in SV</td>
</tr>
<tr>
<td>Decrease in HR</td>
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<tr>
<td>Decrease in TPR</td>
</tr>
</tbody>
</table>

SV, stroke volume; HR, heart rate; TPR, total peripheral resistance.