An agent based model of the vibration-induced arterial growth: feeding the model parameters by cellular tests.

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Summary

Vibration-induced low Wall Shear Stress (WSS) flow inside digital arteries may cause arterial growth and remodeling. In this study, we propose an agent-based model of the WSS-modulated growth, supposedly induced by an intimal hyperplasia phenomenon. The modelled mechanisms depend on the Platelet-derived growth factor BB chain (PDGF-BB) secreted by endothelial cells (ECs) upon exposure to vibration. The PDGF-BB concentrations were obtained from flow experiments on cultured human umbilical vein ECs (HUVECs) exposed to a physiological level of WSS = 3 Pa and a vibration-induced level of WSS = 1 Pa. Results showed higher PDGF-BB level for WSS = 1 Pa. The arterial lumen narrowed around 50% when simulating a vibration exposure of 4 hours a day for 5 years (WSS = 1 Pa).

Introduction

A chronic exposure to Hand-Arm transmitted Vibration (HAV) can cause an arterial growth and remodeling inside digital arteries. In our study, we suppose that the growth is induced by a WSS-modulated intimal hyperplasia phenomenon (IH). Studies have shown that an acute exposure to HAV can decrease the WSS exerted by the blood on the arterial endothelium [1]. A low WSS can promote the EC-secretion of certain mitogens and chemoattractant acting on smooth muscle cells (SMCs), such as the PDGF-BB [2]. We suppose that this secreted PDGF-BB, will alter the dynamics of SMCs. On the long term, this can lead to the development of IH. In this present study, we propose an agent-based model that describes the SMCs dynamics inside the arterial wall during physiological state and for a low WSS resulting from vibration exposure. The secretion of PDGF-BB for different WSS values was investigated using in-vitro flow experiments on HUVECs. The results of the model will allow understanding the effects of the HAV on the onset of vascular pathologies.

Methods

The agent-based model, implemented in NetLogo©, is based on biological laws derived from literature on ECs behaviors when exposed to low WSS. The initial geometry is a normal muscular artery including the endothelium (ECs) and the media layer (SMCs and Extracellular Matrix (ECMs)). The SMCs dynamics were modelled using probabilistic equations that describe biological mechanisms such as the proliferation/apoptosis, the migration and ECMs synthesis/degradation. Starting from an equilibrium state, the model was then disturbed by a WSS value resulting from a vibration exposure. Our model took into account the acute cellular changes and simulated the chronic SMCs dynamics. Experimental data of the PDGF-BB concentrations secreted by HUVECs when exposed to a low WSS were used as input parameters for our model.

Results and Discussion

Results of the cellular tests on HUVECs showed that the ECs secreted almost 50% more PDGF-BB for WSS = 1 Pa (27.93 ± 5.14 pg/ml) than for WSS = 3 Pa (18.50 ± 7.97 pg/ml) ($p < 0.05$, $n = 7$). In addition, our model succeeded in simulating the physiological state, in the absence of vibration and the arterial growth resulting from vibration exposure (Figure 1).

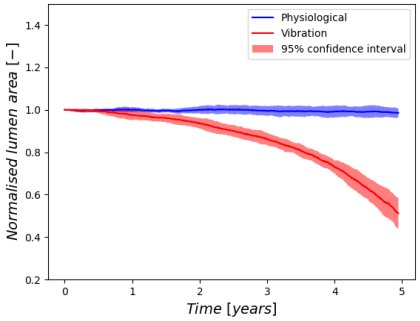

Figure 1. Change in lumen area for physiological and vibration exposure states (average of 5 simulations).

Figure 1 shows a 50% decrease in lumen area upon exposure to vibration, describing the arterial growth after 5 years of 4 hours exposure per day. We only took into account the change in ECs-secretion of PDGF-BB when exposed to a low WSS. However, other mitogens might be released from the SMCs as well and then modulate their dynamics. Our model offers the possibility to include more cellular mechanisms and to study other work conditions with different exposure times.

Conclusions

We presented an agent-based model of the vibration-induced intimal hyperplasia, enriched with experimental data. The model was able to describe the physiological state and predict the arterial growth resulting from vibration exposure.

References

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