Individual differences in the exercise-mediated blood pressure response: Regression to the mean in disguise?

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Loenneke et al. (2014) were interested in what individual differences moderated the exercise-mediated change in blood pressure (BP). They pooled the participants from several different studies and assigned each person to one of three subsamples, (1) those whose BP (systolic, diastolic and/or meant arterial pressure) decreased by more than 10 mmHg, (2) those whose BP increased by more than 10 mm Hg, and (3) those whose BP did not change more than ±10 mm Hg. It was then analysed whether the means of variables measured at baseline differed between the three samples. The primary finding was that those people in sample (1) who showed the largest reduction in BP had a statistically significant and substantially higher mean BP at baseline.

The findings of Loenneke et al. (2014) are contaminated by the regression to the mean (RTM) statistical artefact. The primary finding that was reported could have been obtained with randomly-generated BP data with merely random error introduced between baseline and follow-up measurements (Atkinson et al. 2001; Taylor et al. 2011). Any subsample formed on the basis of the greatest pre-post reduction in BP will tend to have the highest baseline values of BP, sometimes entirely due to the RTM statistical artefact (Taylor et al. 2011). This bias will be introduced as long as there is less-than-perfect repeatability in the measurement of BP.

The RTM artefact predicts that the people who showed the largest exercise-mediated increase in BP would also have the lowest BP measured at baseline. Although this was not the case in Loenneke et al. (2014), there was no covariate-

adjustment in any of the analyses of mean differences. Typically, analysis of covariance (ANCOVA) is used to adjust for the influence of potential confounders. There could be several of these confounders in Loenneke et al. (2014) because data were pooled across several different studies with different interventions. So the estimates of “risk” presented by Loenneke et al (2014) could be biased not only by RTM, but by lack of adjustment for confounders.

The RTM effect can mislead researchers into thinking an intervention has substantial effects in one subsample but not others (Atkinson et al., 2001). The inherent measurement errors associated with BP make it particularly susceptible to RTM effects (Atkinson and Taylor, 2011; Taylor et al., 2010). When extreme subsamples are studied in this way, and there is no matched comparator arm in the study for each subsample, RTM should always be an important issue to address.

Loenneke et al. (2014) highlighted the importance of exploring genetic explanations for their findings. The RTM effect has also been discussed specifically in relation to such gene polymorphism studies on exercise responses (Atkinson et al., 2010). Currie et al. (2014) adopted a similar approach to that of Loenneke et al. (2014). Baseline flow-mediated dilation (FMD%) was compared between groups that differed in the magnitude of exercise-mediated FMD% response. Not surprisingly, the largest reduction in FMD% was associated with higher baseline FMD%. Again, these researcher’s findings are consistent with the RTM effect, rather than any real biologically-mediated individual difference in response. If this approach of analysing baseline differences between “responders” and “non-responders” is to be adopted at

all, then the RTM artefact should be ruled out, either by appropriate randomised comparator samples or by statistical means (Taylor et al. 2010).

References

Atkinson, G., Taylor, C. Normalization effect of sports training on blood pressure in hypertensive individuals: Regression to the mean? Journal of Sports Sciences (2011); 29: 643-644.

Atkinson, G., Taylor, C.E., Jones, H. Inter-individual variability in the improvement of physiological risk factors for disease: Gene polymorphisms or simply regression to the mean? Journal of Physiology, (2010); 588: 1023-1024.

Atkinson, G., Waterhouse, J., Reilly, T., Edwards, B. How to show that unicorn milk is a chronobiotic: The regression-to-the-mean statistical artefact. Chronobiology International (2001); 18: 1041-1053.

Currie K.D., McKelvie R.S., MacDonald R.J. Brachial Artery Endothelial Responses during Early Recovery from an Exercise Bout in Patients with Coronary Artery Disease. BioMed Research International (2014). Article in press, http://dx.doi.org/10.1155/2014/591918

Taylor, C.E., Jones, H., Zaregarizi, M., Cable, N.T., George, K.P., Atkinson, G. Blood pressure status and post-exercise hypotension: An example of a spurious correlation in hypertension research. Journal of Human Hypertension, (2010); 24: 585-592.

Loenneke JP, Fahs CA, Abe T, Rossow LM, Ozaki H, Pujol TJ, Bemben MG. Hypertension risk: exercise is medicine* for most but not all. Clin Physiol Funct Imaging (2014) 34, pp77–81