Online Resource 2 – Effect of AVP distribution volume on [AVP]

Hypovolemia has been shown to be an important factor influencing plasma [AVP] and a reduced body fluid volume triggers a change in the slope of the [AVP]-to-osmolality relationship. In addition, hypovolemia triggers an exponential rise in [AVP], which depends on the reduced volume in percent (Dunn et al. 1973). In this online resource we tested whether these two cases might be caused by a reduction in the AVP distribution volume, or if additional mechanisms are required to account for the increased plasma [AVP].

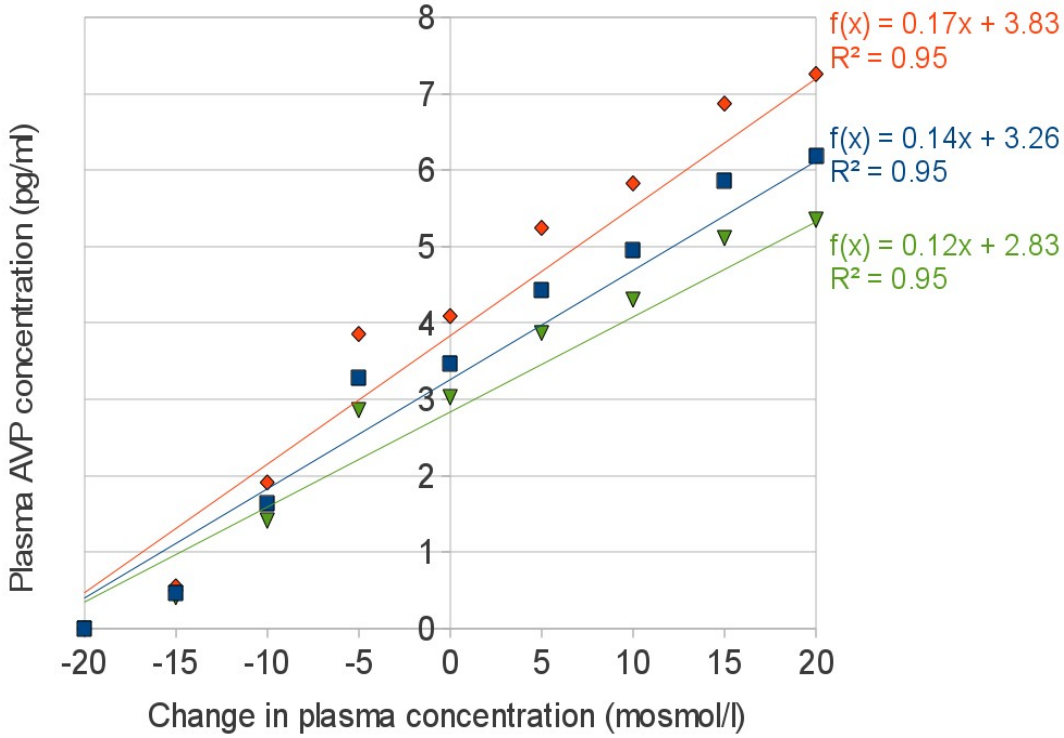

Fig.1: Effect of the AVP distribution volume on plasma [AVP] when osmotic concentration is varied.

This simulation predicted the slope of the [AVP]-to-osmolality relationship in hypovolemia (15% reduction in the AVP distribution volume, 60 ml; orange diamond), in isovolemia (blue square) and in hypervolemia (15% increase in the AVP distribution volume; green triangle). The slope of the [AVP]-to-osmolality was clearly modified (see trend line equations). However, in percent, the change in the simulated slope (+20% slope in hypovolemia) was less important that the change in the slope of the experimental data obtained for an equivalent volume loss (+185%; Figure 6 of Dunn et al. 1973). This discrepancy indicates that the increased slope of the experimental data was not solely caused by a change in volume and that additional active mechanisms stimulating AVP secretion are required.

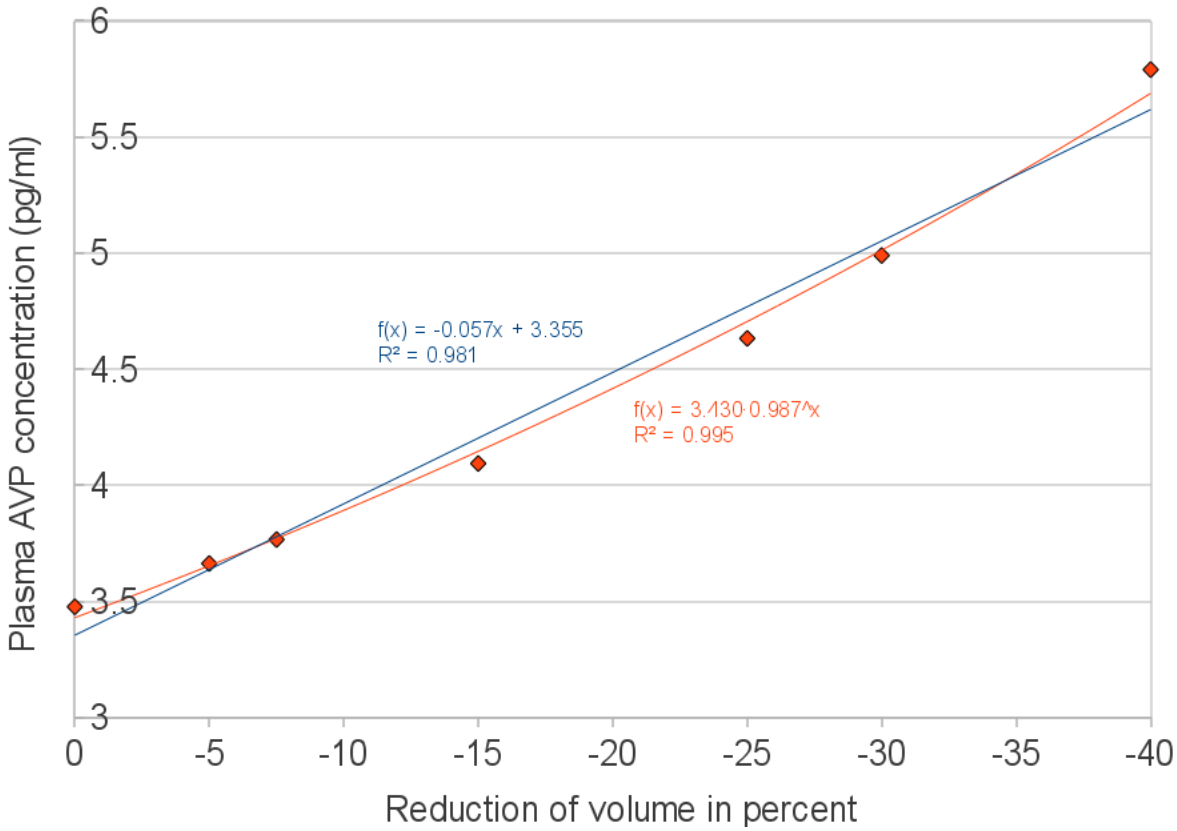

Fig.2: Effect of a reduced AVP distribution volume on plasma [AVP] in iso-osmotic and hypovolemic conditions.

This simulation predicted a weak exponential increase in [AVP] with hypovolemia because R^2 of the linear trend line (0.981) was lower than R^2 of the exponential trend line (0.995). However, the simulated exponential increase in [AVP] due to the distribution volume did not match the experimental data (Figure 7 of Dunn et al. 1973). Indeed, the simulation of a 20% reduction in the distribution volume triggered a weak increase in [AVP] from 3 to 4.5 pg/ml. Contrastingly, a similar decrease in body fluid volume in the rat triggered a massive increase in [AVP] from 1.3 to 40 pg/ml.

Taken together, the huge discrepancy between simulation and experimental data suggests that AVP secretion caused by a change in the body fluid volume is not only a consequence of a passive increase in [AVP] due to the reduction of the AVP distribution volume but is caused by active mechanism(s) protecting the organism from volume loss.

Reference:

Dunn, F. L., Brennan, T. J., Nelson, A. E., & Robertson, G. L. (1973). The role of blood osmolality and volume in regulating vasopressin secretion in the rat. *Journal of Clinical Investigation, 52*, 3212-3219.