COAT Platelets Under Alarm

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Thromb Haemost 2021;121:1267.

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Epinephrine (adrenaline) is a hormone synthesized by the adrenal gland medulla and by neurons. It is released following physical activity, mental stress, or other conditions associated with sympathoadrenal activation.¹ Platelets exhibit α_2A adrenergic receptors making them susceptible to systemic epinephrine release. In this context, epinephrine can influence platelet reactivity under systemic stress.

Epinephrine has a rather indirect mode of action by amplifying the response to other agonists.² In this issue of *Thrombosis and Haemostasis*, Aliotta et al³ investigated the additional impact of epinephrine on procoagulant collagen and thrombin coated (COAT) platelets. COAT platelets are formed after co-stimulation of protease-activated receptors and glycoprotein VI, e.g., with thrombin and convulxin, respectively. COAT platelet formation is associated with phosphatidylserine (PS) exposure and a sustained cytosolic Ca^{2+} increase and affects a higher proportion of large platelets.⁴

The authors confirm that epinephrine stimulation alone does not affect free cytosolic Ca^{2+} and elegantly show that it dose dependently reduces free cytosolic Ca^{2+} of thrombin + convulxin stimulated platelets. This decreases the proportion of PS-positive COAT platelets and increases the proportion of PAC-1-binding aggregatory platelets. Thus, very high doses of 1,000 μM epinephrine switch the platelet response from a procoagulant phenotype toward aggregation.

Albeit such high epinephrine concentrations appear less likely to occur in vivo, Aliotta and colleagues discuss that platelets respond to a 15- to 55-fold lower epinephrine concentration in vivo. Extrapolating their data, such a switch could appear at doses of 6 μM , coming near to systemic

concentrations achieved after epinephrine injection. Further, it is unknown which concentrations of epinephrine appear in the microenvironment around vascular injuries, where platelets begin to act. This deserves future investigations. Meanwhile, it is a rational hypothesis that epinephrine modulates procoagulant COAT and pro-aggregatory platelet formation when the organism is alarmed or when patients receive high doses of catecholamines.

Funding

S.H. is funded by Deutsche Forschungsgemeinschaft (DFG, German Research Foundation; Projektnummer 374031971-TRR 240.

Conflict of interest

None declared.

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received

July 23, 2021

accepted

July 26, 2021

published online

August 24, 2021

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Georg Thieme Verlag KG,
Rüdigerstraße 14,
70469 Stuttgart, Germany

DOI <https://doi.org/10.1055/s-0041-1735190>.
ISSN 0340-6245.