Dopamine Microdialysis is Influenced by Probe Implantation Trauma

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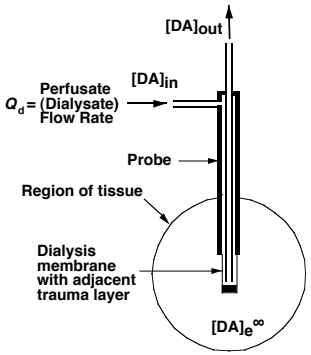
Abstract

Although microdialysis is widely used to sample endogenous and exogenous substances *in vivo*, interpretation of the results obtained by this technique remains controversial. Tissue trauma from probe implantation could be a source of confounding effects. To address this issue, an existing quantitative mathematical model for microdialysis[1] was modified to incorporate a traumatized tissue layer interposed between the probe and surrounding normal tissue. The revised model has been applied to the specific case of dopamine (DA) measurements in the brain extracellular microenvironment[2]. DA uptake avidity from the extracellular space in anesthetized rat striatum obtained by the concentration difference (no-net-flux) microdialysis technique appears to be lower than the avidity determined by fast-scan cyclic voltammetry. Because the relatively small size of the voltammetric microsensor produces little tissue damage, the discrepancy is likely to be a consequence of the microdialysis probe implantation trauma. According to the model, a traumatized layer with reduced uptake and no release can reconcile discrepancies between microdialysis and voltammetry results. The model predicts *inter alia* that this trauma layer would lead microdialysis to underestimate the DA extracellular concentration in the surrounding normal tissue. Implications for microdialysis of other solutes are currently under investigation.

[1]PM Bungay, PF Morrison, and RL Dedrick, Steady-state theory for quantitative microdialysis of solutes and water *in vivo* and *in vitro*. *Life Sci*, 46:105-19, 1990.

[2]PM Bungay, P Newton-Vinson, W Isele, PA Garris and JB Justice, Jr., Microdialysis of dopamine interpreted with quantitative model incorporating probe implantation trauma. *J Neurochem* 86: 932-946, 2003.

In Vivo Microdialysis Nomenclature



Extraction Fraction:

$$E_d = \frac{[DA]_{in} - [DA]_{out}}{[DA]_{in} - [DA]_e^{app}},$$

where $[DA]_e^{app}$ is an apparent extracellular DA concentration with contributions from trauma layer and surrounding tissue.

Relative Recovery:

$$R = \frac{[DA]_{out}}{[DA]_e^{\infty}} \text{ for } [DA]_{in} = 0,$$

where $[DA]_e^{\infty}$ is the extracellular concentration of endogenous DA in normal tissue.

1. Discrepancy between estimates for basal level of extracellular DA in rat striatum:

Microdialysis*, $[DA]_e \sim 10$ nM

Voltammetry#, $[DA]_e \sim 500$ nM

*AD Smith & JB Justice, Jr, J Neurosci Meth 54: 75-82, 1994

#NV Kulagina, MJ Zigmond & AC Michael, J Neurosci 102: 121-128, 2001

2. Discrepancy between estimates of the rate constant for DA clearance from interstitium of rat striatum:

Microdialysis: $k_e^{app} \sim 5\ s^{-1}$

Voltammetry: $k_e \sim 15\ s^{-1}$

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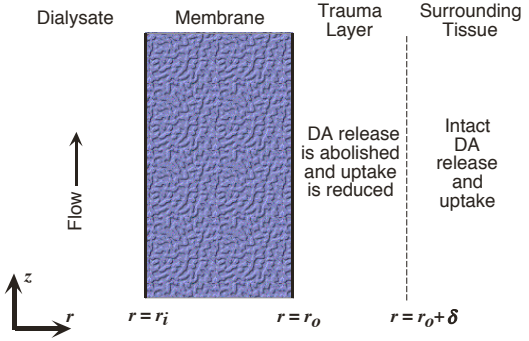
3. Change in DA concentration in dialysate or adjacent tissue during electrically evoked release is undetectable by voltammetry, except in presence of uptake inhibitor*, suggesting:

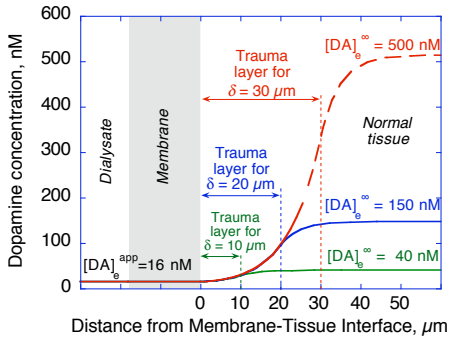
- Absence of DA release in traumatized tissue,
- DA diffusing from surrounding tissue does not arrive at microdialysis probe because of clearance (uptake, ...) in trauma layer.

H Yang, JL Peters, A Michael, J Neurochem 71:684-692, 1998

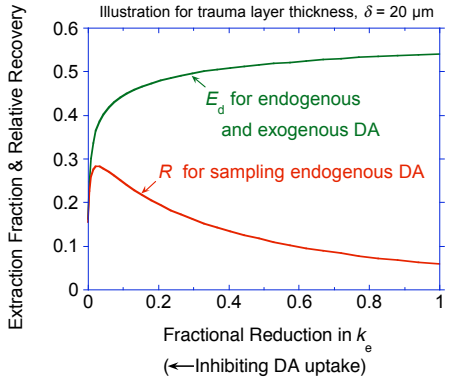
4. Hypothesis: DA release is abolished and uptake is impaired in traumatized tissue adjacent to probe



5. Mathematical model based on this hypothesis predicts no-net-flux intercept concentration, $[DA]_e^{app}$, is less than the normal tissue concentration, $[DA]_e^{\infty}$, and the difference is a function of the unknown thickness of the trauma layer, δ



6. Consequently, relative recovery (R) for endogenous DA would be lower than E_d. Also, uptake inhibition will increase R, but decrease E_d



7. Conclusions

- Trauma hypothesis permits quantitative reconciliation of microdialysis and fast scan cyclic voltammetry measurements.
- Microdialysis may underestimate DA extracellular concentration in the normal tissue and overestimate DA relative recovery.