Dopamine Uptake Capacity of Platelets From People At Risk For Huntington's Chorea

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SUMMARY: *Dopamine (DA) uptake by platelets from 41 patients at risk to develop Huntington's chorea was assayed and compared to controls. The DA uptake was significantly higher in the at risk group. However, the at risk group did not separate into two distinct subgroups, which reduces the usefulness of the assay as a disease prognosticator.*

RÉSUMÉ: *L'uptake (captation) de la dopamine dans les plaquettes de 41 patients sous risque de chorée de Huntington a été et comparé à celui d'un groupe contrôle. L'uptake de dopamine est significativement plus élevé dans le groupe sous risque. Cependant ce groupe ne se sépare pas en deux sous-groupes distincts, ce qui rend moins utile comme pronostic le test propose.*

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INTRODUCTION

In our recent report (McLean & Nihei, 1980), we confirmed the previous observation that the Dopamine (DA) uptake capacity of platelets from Huntington's chorea (HC) patients is greater than the uptake in platelets from normal controls (Aminoff et al, 1974; McLean & Nihei, 1977). The uptake capacity is the amount of DA incorporated into platelets at equilibrium. If the DA uptake abnormality is present in the pre-symptomatic stage of HC, 50% of the patients at risk to develop HC should show increased uptake as HC is transmitted by an autosomal dominant gene. To examine this possibility, we measured the DA uptake capacity of platelets from offspring of 10 HC patients. The results suggest that the DA uptake abnormality exists in the pre-symptomatic state.

MATERIAL AND METHODS

From 10 families with an HC parent, 41 (19 female and 22 male) offspring, age 7 to 40 years (mean age 23), volunteered their blood for examination. None of these at-risk individuals exhibited symptoms or signs of HC. All offspring were sampled in 6 families but geographical impracticalities excluded 5 individuals from the other 4. Blood was obtained following a fast lasting at least ten hours. The normal control blood was obtained from 36 volunteers, age 11 to 55 years (mean age 33).

The procedures of the platelet rich plasma (PRP) preparation and the assay of DA uptake capacity have been described previously (McLean & Nihei, 1980).

RESULTS AND DISCUSSION

The mean DA uptake capacity of platelets in people at risk and normal controls is summarized in Table 1. An increased mean DA uptake capacity is observed in the people at risk group for DA substrate concentrations of 0.25 and 0.5 mM ($p < 0.01$) but less significantly for 0.10 mM ($p < 0.02$).

Theoretically, within the at risk group, there should be two distinct subgroups; normals and those who will develop the disease. Can these subgroups be identified? Figure 1 shows the distribution of individual uptake capacity. Uptake values are grouped in increments of 0.05 nmoles DA uptake per 10^8 platelets. If two subgroups exist, a bimodal distribution pattern should emerge. Such a pattern is not present. A bimodal distribution could be masked by the large standard deviation and relatively small difference in the two groups, causing a large overlap, or there may not be two subgroups and this may be the normal uptake distribution curve, peculiar to HC families.

Several points are worth noting. Individuals with high uptake values at one DA substrate concentration had high uptake at the other concentrations. High uptake levels in the patient at-risk group were not peculiar to families, sex or age, but occurred randomly. The mean age in controls is higher than in the at risk group but we have shown previously that DA uptake is not age related.

Because the DA uptake capacity in patients at risk did not separate clearly into two subgroups, despite showing a higher mean uptake capacity, the assay is less promising as a prognosticator of subsequent disease. However, refinement may improve the assay. We have demonstrated (unpublished data) that human platelets take up DA via two apparently independent mechanisms. One is blocked by NH_4Cl which collapses the pH gradient across the

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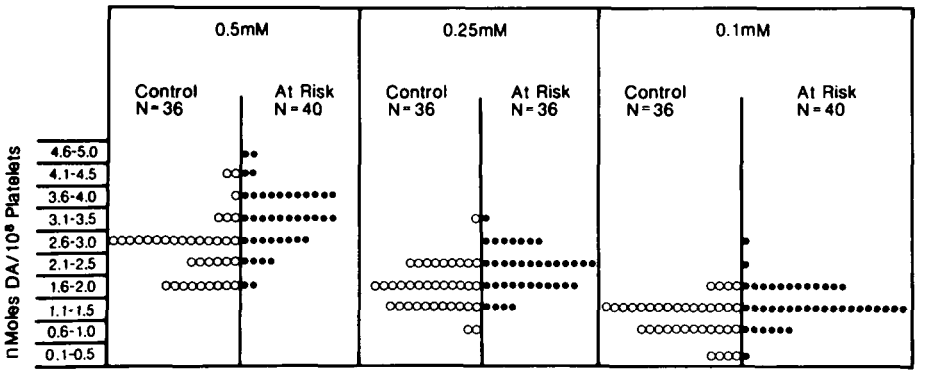

Figure 1. — Distribution of dopamine uptake capacity of platelets from normal controls (open circles) and people at risk (closed circles) to develop HC. Each circle represents the average of duplicate assays on single blood sample rounded to the first decimal place, and plotted along the vertical axis in increments of 0.5 nmoles per 10^8 platelets. For technical reasons, a few specimens were not analyzed at each substrate concentration.

TABLE I

*Dopamine Uptake Capacity**

mM DA added	0.50	0.25	0.10
	Mean S.D.	**Mean S.D.**	**Mean S.D.**
Normals	2.62 ± 0.66 N = 36	1.77 ± 0.50 N = 36	1.18 ± 0.35 N = 36
At Risk	3.25 ± 0.71 N = 40	2.15 ± 0.53 N = 36	1.40 ± 0.40 N = 40
Difference	0.63	0.34	0.22
P	< 0.001	0 < 0.01	< 0.02

* The uptake capacity is expressed in nmoles of dopamine incorporated per 10^8 platelets in one hour at 37°.

membrane (Nichols & Deamer, 1976). This process is saturable at DA substrate concentrations near 0.1 mM. The second mechanism is not affected by NH_4Cl, is not saturable and DA accumulates linearly as the substrate concentration increases. Both uptake mechanisms are inhibited by haloperidol (Solomon et al, 1970). We have not identified the mechanism which accounts for the increased DA uptake by platelets from patients with HC. By isolating each uptake system, it may be possible to improve the sensitivity of the DA uptake assay, and subsequently arrive at a more promising prognosticator of disease.

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