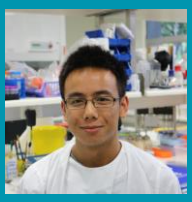

Peripheral Innate Immunity in Huntington's Disease

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Introduction

Huntington's Disease (HD) is a neurodegenerative disease caused by autosomal dominant poly-glutamine (CAG) mutations in the huntingtin gene. Currently, there are no disease modifying treatments for this condition, but emerging evidence suggests that HD is associated with a neuroinflammatory response that exacerbates the underlying condition and offers a unique opportunity for drug development. However, the role of the peripheral innate immune system in HD remains under investigated.

Research objectives

Thus, we sought to immunophenotype the innate immune system in patients with HD and to correlate these findings with disease progression.

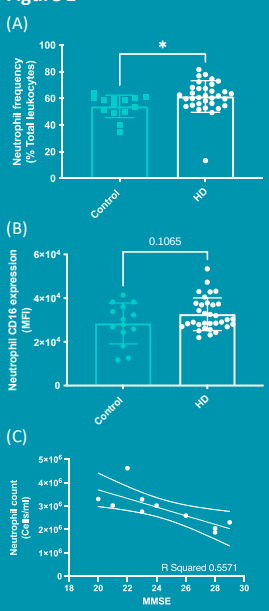
Methods

We performed flow cytometry on whole blood samples from patients with manifest HD (n = 33) and healthy controls (n = 14). Specifically, we measured total and subset granulocyte and monocyte counts and their expression of certain activation markers e.g. CD16. We then correlated these findings with genetic and clinical markers of disease severity/progression including patient CAG length; CAP score, a product of CAG length and age; total motor Unified Huntington's Disease Rating Scale (UHDRS) score, a composite motor function score; and mini-mental state (MMSE) score, a global score of cognitive function.

Results

Our study found predominantly granulocytic changes in the innate immune systems of patients with HD. Indeed, patients had increased neutrophil frequency ($p < 0.05$) (fig. 1A) with signs of enhanced maturity in the form of elevated CD16 expression ($p = 0.11$) (fig. 1B). Moreover, neutrophil counts were found to correlate with disease progression as measured by MMSE scores (fig. 1C).

Figure 1



By contrast, patients with HD had markedly reduced eosinophil counts ($p < 0.01$) that correlated with CAP score (figure 2). However, total and subset monocyte counts were not significantly different between patients with HD and healthy controls, but the proportion of pro-inflammatory classical monocyte counts did correlate with total motor UHDRS (figure 3).

Figure 2

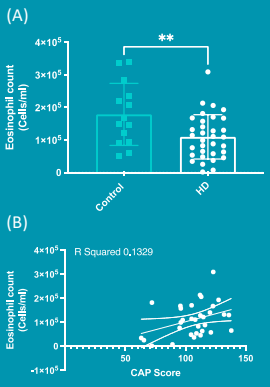
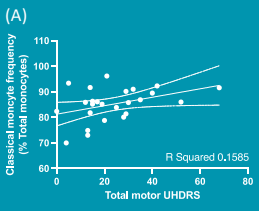


Figure 3



Discussion

Our findings suggest that HD is associated with a granulocytic innate immune response. Indeed, patients with HD had elevated neutrophil frequency with evidence of enhanced maturation, which is consistent with previous reports of patients having increased plasma levels of granulocyte-macrophage colony stimulating factor. Moreover, the eosinopenia that was seen in the early-mid stages of disease was most likely reflective of active recruitment to degenerating tissues as patients in these categories have increased levels of eotaxin 1/3 in their plasma. In contrast, we did not observe any overt monocytic changes in patients with HD, but this may due to the moderate sample size of this study.

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