The Role of Saccades in Monitoring Progression of Huntington's Disease

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Prevalence & Genetics

Huntington's disease (HD) is an autosomal dominant neurodegenerative disease[1]. Genetically, HD patients have an extended CAG repeat sequence in the Huntington gene[1].

Table 1. *Worldwide Prevalence of HD*[1].

Area	Cases per 100,000
Worldwide	2.71
Asia	0.40
North America, Europe, Australia	5.70
Lake Maracaibo	700

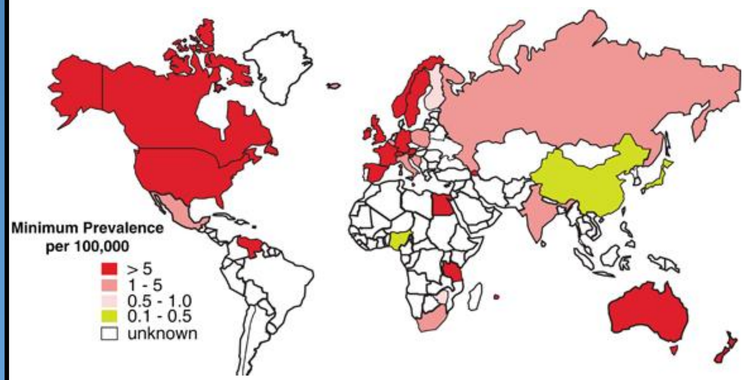

Figure 1. World estimates of Huntington's Disease[2].

Mechanisms of Neurodegeneration

Overstimulation of glutamate receptors, especially the NMDA receptors may cause HD neurodegeneration[3]. In HD patients, wild type astrocytes increase glutamate production and release, activating NMDA receptors[4]. NMDA receptor overstimulation allows higher influx of Ca^{2+} ions[3].

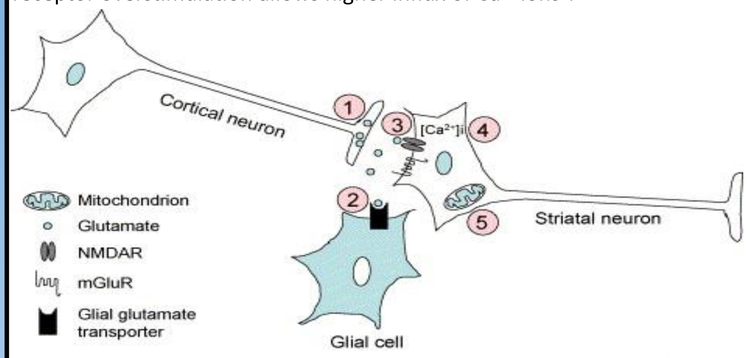

Figure 2. Illustration of possible contributing points of excitotoxicity[3].

Mitochondria in HD positive individuals cannot maintain homeostasis of cytosolic Ca^{2+} and release apoptotic factors into the cytosol[3,4]. Interestingly, this mitochondrial malfunction is also seen in peripheral tissues[3]. In theory, these cellular malfunctions occur throughout life but appear as symptoms only when self-defence mechanisms can no longer keep up with damage[3].

Saccadic Deficiencies & Disease Severity

Individuals with HD have slower and more variable saccadic reaction times and higher incidence of movement errors than age and gender matched controls[5]. As seen in Figure 3, HD patients make more errors in anti-saccadic movements and with increasing delays than controls do[5]. Combined timing and direction errors in saccadic movements in delayed anti-saccadic movement tasks are highly correlated with disease severity ($P<0.01$)[5].

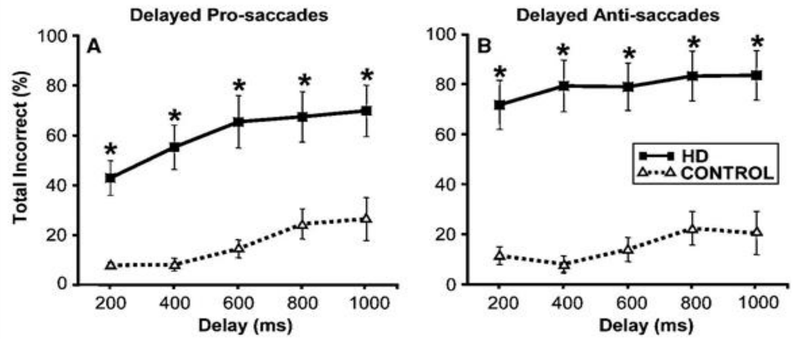

Figure 3. Errors made in delayed pro and anti-saccadic tasks[5].

These measures are sensitive enough to detect deficiencies in pre-symptomatic and pre-diagnosed HD gene carriers and may be more effective than the currently employed motor test[6].

Saccadic Deficiencies & Neurodegeneration

Two types of neurons were identified when neuronal activity was measured in the caudate nucleus of rhesus monkeys: one reacted to pro and another in anti-saccades (as seen in Figure 4)[7].

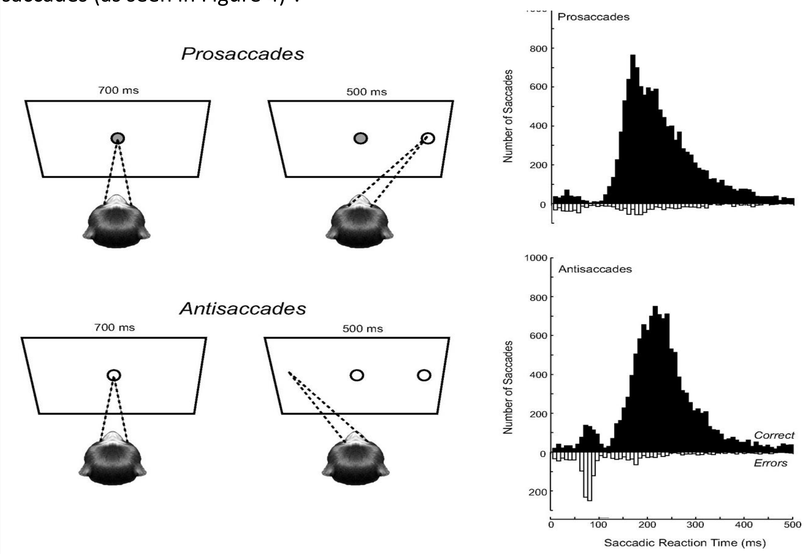

Figure 4. Two types of CN neurons respond to either pro or anti-saccades[8]

The neurons activated in anti-saccades act through the indirect basal ganglia pathway to inhibit pro-saccade neurons in the superior colliculus[7]. The degeneration of these caudate nucleus neurons seems to be responsible for the inability of HD patients to inhibit pro-saccades[7].

Conclusions

Huntington's disease is a lethal, progressive disease for which there is no cure[8]. Pharmacological symptomatic treatments are common, but newer research focuses on boosting mitochondrial function supplements like coenzymes, creatine, and even medical marijuana[9]. Electrooculography, as seen in Figure 5, may offer an inexpensive, portable means to track disease progress in studies directed towards delaying HD onset or slowing progression[9].

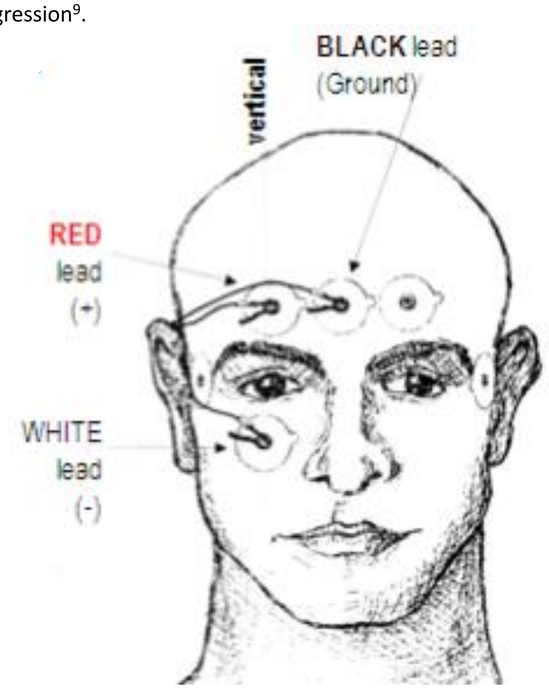

Figure 5. Electrode placement for electrooculography measurement[9].

References

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