INTERHEMISPHERIC PROCESSING IN HYPERKINETIC MOVEMENT DISORDERS

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Background and Rationale

Changes in interhemispheric connectivity in Huntington's Disease (HD) have been only recently investigated and little is known about their temporal relation with clinical features or grey matter atrophy: callosal disruption could contribute both to cognitive dysfunction and impairment of associative functions (Rosas et al. , 2010) and likely occurs many years before clinical onset, along a posterior-to-anterior direction (Phillips et al. , 2013). Here, we evaluated changes in ipsilateral Silent Period (iSP: onset latency, iSPOL, and duration, iSPD) and Transcallosal Conduction Time (TCT) in HD patients and correlated electrophysiological findings with mutational load and motor score (UHDRS-I). Data were then compared with those obtained from healthy volunteers and patients with idiopathic laterocervical dystonia (LCD). In the recent past, also in cervical dystonia electrophysiological evaluation of limb muscles have revealed a widespread disease (Kanovsky, 2003; Amadio et al., 2014).

Materials and Methods

Seven drug-free patients were enrolled, a number in line with previous papers studying early HD patients (Schippling et al. , 2009). They had undergone genetic testing, which was diagnostic in all (CAG number ≥ 40). The mean duration of symptoms was about one year (15.1 ± 5.8 months). Electromyographic recordings were made from the ipsilateral abductor pollicis brevis muscle. A Super Rapid Transcranial Magnetic Stimulator connected to a eight-shaped focal coil with wing diameters of 70 mm was used.

iSP onset was defined as when the post-stimulus EMG fell continuously (for at least 10 ms) in a window 30–60 ms after the stimulus. Subjects had to maintain a slight, unilateral, voluntary muscle contraction by means of an EMG visual feedback system. TCT was calculated by subtracting the shortest contralateral MEP onset latency from the iSP onset latency (Petitjean and Ko, 2014).

Patient	1	2	3	4	5	6	7
Age	43	45	50	51	40	42	47
Sex	M	F	F	M	F	M	F
MMSE	26/30	25/30	27/30	25/30	24/30	25/30	27/30
CAG-length	41	44	40	44	47	45	42
UHDRS -I (motor)	14	17	11	15	20	18	14
Disease Burden (DB)	236.5	374	225	433.5	460	399	258.5
Mirror Movements	-	+	-	-	+	-	-

Table 1 – Demographic and clinical features in HD patients

Patient	1	2	3	4	5	6	7
iSPOL	44.6	46.2	39.6	47.3	50.8	49.1	42.2
iSPD	13.6	10.3	17.5	11.0	10.2	9.3	16.1
TCT	25.7	30.4	24.0	30.3	33.2	31.8	22.5

Table 2 – Electrophysiological data in HD patients

Results

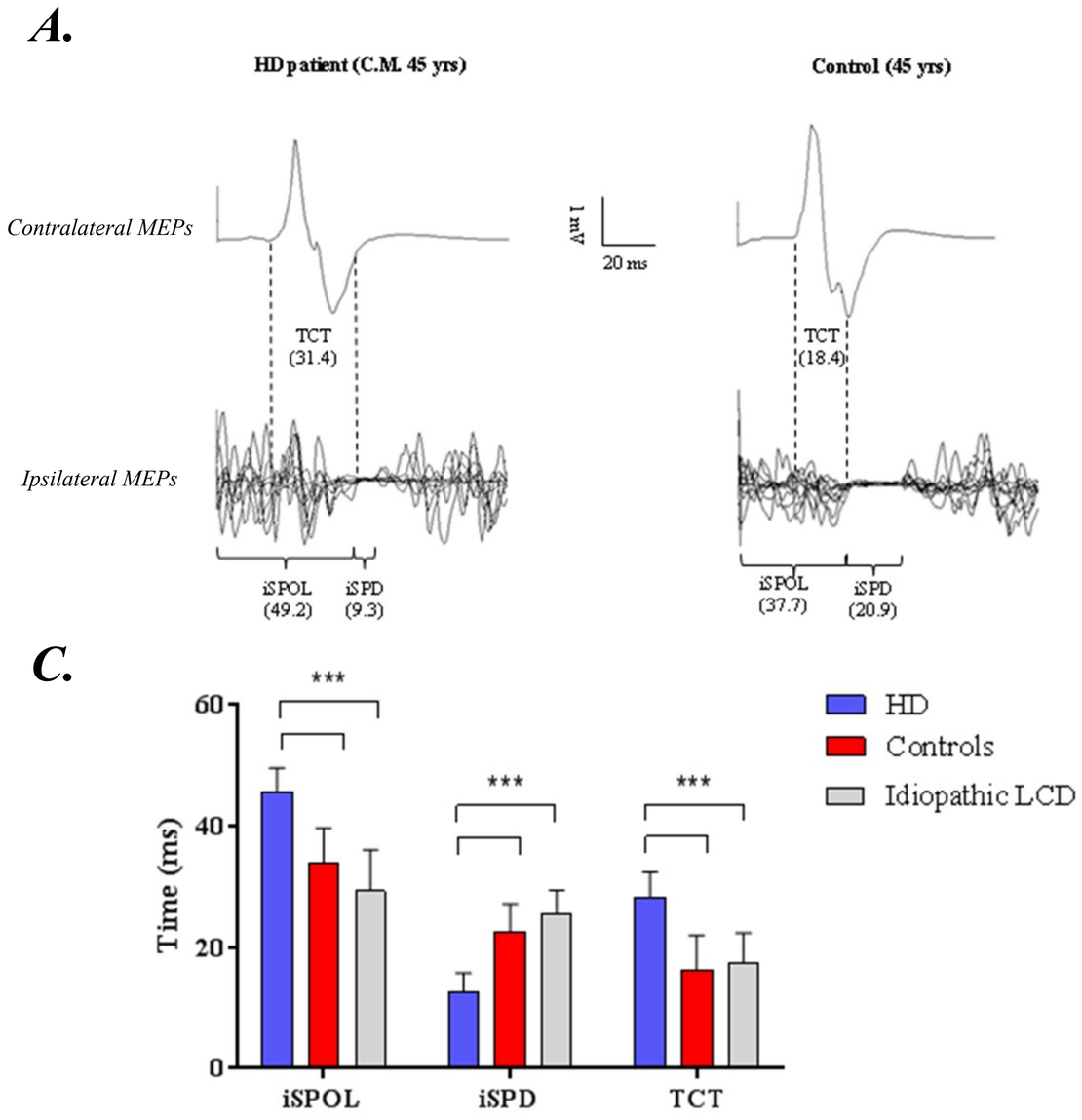

Figure 1 *– **A.** Comparison between traces recorded from a HD patient and an healthy volunteer. Upper traces show the contralateral motor evoked potential, while bottom ones electromyographic recordings when the ipsilateral motor cortex was stimulated. In HD patient, there was a significant reduction in iSPD, paralleled by a lengthening of iSPOL and TCT. Note that some MEPs were recorded in the ipsilateral EMGs; although iMEPs are commonly observed in only a minority of subjects and mainly for proximal arm muscles, they could be found also for hand muscles during voluntary contraction at stimulation intensities quite similar to those we used (Chen et al., 2003). **B.** Average and rectification of ipsilateral EMGs in patients (HD: blue; LCD: grey) and controls (red). **C.** Histogram showing significant differences between HD and controls in term of iSPOL, iSPD and TCT (*** $p < 0.001$).*

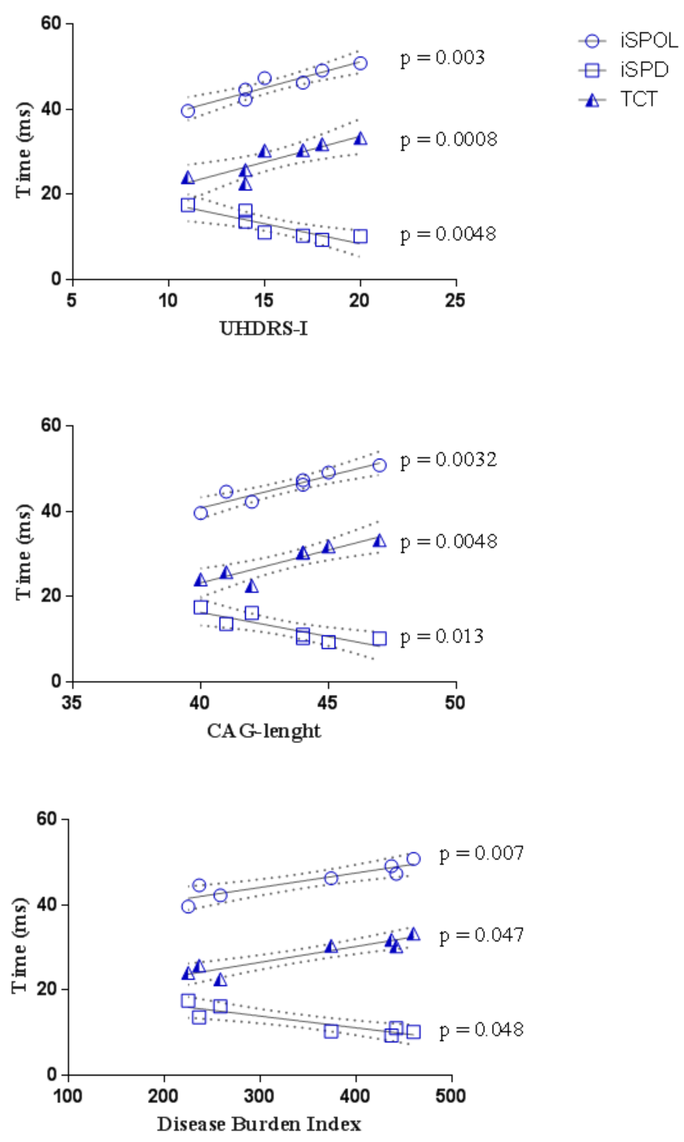

Figure 2 *– Correlations between electrophysiological data (iSPOL, iSPD, TCT), motor scores and mutational load. Note that iSPOL and TCT are directly correlated with CAG-length and motor score, as well as with the Disease Burden Index, while iSPD shows an inverse correlation. Correlation lines (black) and error bars (dotted lines) are shown.*

Discussion and Conclusions

- **Our data proved that interhemispheric processing is impaired in early HD, but not in idiopathic cervical dystonia, and significantly correlates with clinical and genetic data**.

- **Our results could have implications for the disruption of both sensorimotor integration and voluntary motor control in HD**. Immediately before voluntary movements, interhemispheric interactions are likely responsible both for the temporary inhibition of ipsilateral primary motor cortex (M1) and the increased excitability of contralateral one (Leocani et al. , 2000). Concurrently, especially during non-dominant hand movements, enhanced interhemispheric inhibition from the ipsilateral hemisphere suppresses superfluous activation arising from the contralateral cortex (Kobayashi et al. , 2003). These mutual interactions may be lost in symptomatic HD, thus contributing to hyperkinesias.

- **No study exists to date about the use of TMS to explore interhemispheric function in the whole field of hyperkinetic movement disorders**; this approach may lead to a better knowledge of disease mechanisms, also in pre-symptomatic patients and other hyperkinetic movement disorders.