C Clinical characteristics

C.1 HUNTINGTON'S DISEASE TOOLKIT: META-ANALYSIS PROVIDES BENCHMARKS FOR IDENTIFYING PROMISING INDICATORS OF PROGRESSION IN PREDIAGNOSIS AND EARLY HUNTINGTON'S DISEASE

[1]S Queller, [1,2]J Stout, [1]A Tomusk, [2]C Milchman. *[1]Department of Psychological and Brain Sciences, Hillcrest Psychology Research Center, Indiana University, 674 East Cottage Grove Avenue, Mail Box 3, Bloomington, IN 47408, USA; [2]School of Psychology, Psychiatry and Psychological Medicine, Room 534, Building 17 Clayton Campus, Monash University, Victoria 3800, Australia*

Background: Identification of tasks that reliably mark the approaching onset and progression of Huntington's disease (HD) or the slowing of progression in response to treatment intervention can facilitate the discovery of useful treatment interventions.
Aims: The HD Toolkit meta-analysis provides benchmark effect sizes from well studied tests of neurocognitive function. We use these benchmarks to evaluate effect sizes for tracing and movement to target tasks.
Methods: We compared the effect sizes from published reports of tracing and movement to target tasks to benchmark effect sizes from published reports of four tasks: Stroop, Symbol Digit Modalities Test, Verbal Fluency, and Speeded Tapping. We computed cross-sectional effect sizes as the mean difference in performance between an HD group and controls, divided by the pooled standard deviation. Effect sizes were corrected for small sample sizes and were coded so that negative numbers indicated worse performance in the HD group compared with controls.
Results: In early HD (<7 years since onset), cross-sectional effect sizes in tracing and movement to target tasks were up to double the effect sizes of the most sensitive of the benchmark tasks (eg, Lemay *et al*, 2005, Circle Tracing Hedges $g = -3.43$ versus Symbol Digit Modalities Test $g = -1.69$). In prediagnosis HD, the cross-sectional effect size in a movement to target task was triple that of the effect size of the most sensitive of the benchmark tasks (Smith *et al*, 2000, $g = -1.63$ versus Speeded Tapping $g = -0.56$). Task variants that revealed movement progress on a remote monitor or in a mirrored fashion and measures that monitored ability to correct a deviation from the intended course of movement seemed particularly sensitive.
Conclusions: Although available evidence is minimal, tracing and movement to target tasks warrant longitudinal study to assess sensitivity as markers of disease progression and treatment effectiveness. The HD Toolkit provides a means to set benchmarks for identifying additional promising tasks.

C.2 COGNITIVE FUNCTION IN PRESYMPTOMATIC HUNTINGTON'S DISEASE: A DOUBLE-BLIND COMPARISON BETWEEN CARRIERS AND NON-CARRIERS IN NORWEGIAN INDIVIDUALS

[1]M van Walsem, [2]L Retterstol, [3]K Sundet, [2]Ø Sundseth. *[1]National Hospital of Norway, Sognsvannsveien 20, 0027 Oslo, Norway; [2]Ullevål University Hospital, Kirkeveien 166, 0104 Oslo, Norway; [3]University of Oslo, Boks 1072 Blindern, 0316 Oslo, Norway*

Background: The onset of symptoms in Huntington's disease (HD) shows great variability, making accurate determination of the start of clinical HD difficult. Less characteristic symptoms may appear earlier than motor symptoms. Healthy gene carriers provide the opportunity to examine the earliest signs of HD. Insight into subclinical signs will be critical for the development of clinical trials. Previous studies have given conflicting results.
Aim: The aim of the study is to compare cognitive performances between carriers and non-carriers in a Norwegian cohort. In addition, the influence of CAG repeat sizes and proximity to disease onset on cognitive decline was investigated.
Methods: A neuropsychological test battery covering the various cognitive domains was administered and population characteristics were recorded. Statistical analyses of characteristics were completed with analysis of variance and the χ^2 test. Group comparisons were executed with multivariate analyses of variance and co-variance. In addition, the relationships between CAG repeat size and proximity to the onset on cognitive performances were investigated by calculating correlations.
Results: No differences between carriers and non-carriers were revealed. However, a tendency towards lower performance on one neuropsychological variable and lower numeric mean performances were found. Group comparisons for CAG repeat sizes showed no significant differences and only two weak associations. Carriers closer and further from onset tended to differ only on dexterity of the non-dominant hand. Furthermore, some weak and some strong associations with cognition and proximity to onset were revealed.
Conclusions: Although not significant, carriers tend to perform less well than non-carriers. This is potentially caused by subtle cognitive decline that is insufficiently detectable by conventional cognitive assessments. Furthermore, there appears to be no or only a slight influence from CAG repeat size on cognition, whereas proximity to onset clearly has stronger influence.

C.3 EXECUTIVE FUNCTIONS IN HUNTINGTON'S DISEASE

NJ Müller, AK Hödl, BJ Herranhof, RM Bonelli. *[1]Medical University Graz, Auenbruggerplatz 31, 8036 Graz, Austria*

Huntington's disease (HD) is a hereditary and progressive disease of the central nervous system and neuropsychological deficits are a main feature of HD. The executive functions include high-level mental activities such as motor control and programming, mental control, personality and emotion, fluency, creativity and planning. Planning is defined as the ability to organise cognitive behaviour in time and space. Deficits in these functions have been categorised as disorders of the executive system.

52 genetically confirmed patients (30 men, 22 women, age 46.9 ± 11.5, CAG repeats 45.9 ± 4.4) were tested with two different test batteries (Tower of London TL-D and Behavioural Assessment of Dysexecutive Syndrome (BADS)). The patients were divided into clinical stages 1–4 (Shoulson, 1979) and the results were compared separately.

The German version of the well-known test Tower of London TL-D measures planning abilities and the speed and accuracy of thinking. For this test, the patient is instructed to move three different coloured balls to match a target configuration by using a minimum number of moves. The BADS is a comprehensive neuropsychological assessment battery designed for "ecological validity" and other measures of frontal executive functions. The BADS is a test battery of six different element tests to investigate deficits in planning ability and "everyday" difficulties. The results are presented at the congress.

C.4 SYNTACTIC CHANGES IN HUNTINGTON'S DISEASE

[1]N Berchtold, [1]V Thiemann, [1]H-P Gadler, [2]AK Hödl, [2]H-P Kapfhammer, [2]RM Bonelli. *[1]Institut of Linguistics Graz, Merangasse 70, Graz, Austria; [2]University Clinic for Psychiatry Graz, Auenbruggerplatz 31, Graz, Austria*

Introduction: Although general descriptions of Huntington's disease (HD) have traditionally stated that this disease is not associated with language changes, an increasing number of studies have identified language deficits in patients with HD, even when they are in the early stages of the disease. The purpose of this study was to investigate language functions in HD compared with

healthy controls and to prove the debated role of the basal ganglia in language functions.

Method and Materials: 20 patients (12 men, eight women) with HD participated in the study. The control group comprised 20 age, sex and education-matched healthy subjects. A specific language screening was constructed that served to assess a wide range of language functions. Syntactic knowledge was tested in production and comprehension. The productive task of the syntactic screening consisted of arranging parts of a sentence in a grammatically correct way and generating a correct sentence out of three given parts. The second part of the screening was designed to probe divergent syntactic comprehension mechanisms with a sentence–picture matching task.

Results: Syntactic abilities are severely affected in patients with HD compared with healthy controls. Results suggest that HD patients experience difficulty on more demanding syntactic tasks, such as for example with semantically reversible sentences.

Conclusion: A correlation of these data with disease progression and degeneration measures of the basal ganglia is needed to disclose language functions of the basal ganglia. Additional correlations with age, sex and education scores will follow.

C.5 SPEAKING IN FRAGMENTS: GRAMMATICAL ASPECTS OF HUNTINGTON'S DISEASE SPOKEN LANGUAGE

A-W Heemskerk. *Huntingtoncentre Overduin, Nachtegaallaan 5, 2225 SX Katwijk, The Netherlands*

Background: When investigating Huntington's disease (HD) spoken language the main focus is on the physical effects of dysarthria. In this study the attention was shifted towards the grammatical aspects of HD spoken language. In the literature little attention has been paid to semantic/syntactic aspects, although there is some evidence that the spoken language of HD patients detoriates because of language problems. Therefore we chose to investigate the grammatical aspects of HD spoken language.

Aims: The aims of this study were therefore to investigate syntactic grammatical problems in HD patients.

Method: As there is no grammatical test available particularly for HD patients, the SAN test, a standardised Dutch language aphasia test was used to investigate the spoken language of 14 HD patients. The results were analysed and categorised into three kinds of grammatical errors.

Outcomes: The results on the grammatical test were used to determine the nature of the grammatical errors made by the HD patients. As was expected most errors were due to omissions. 48% of all uttered sentences in the test were ungrammatical. Of these ungrammatical sentences:

- 75% were incorrect on word order
- 71% were incorrect because of omissions of the subject, verb and/or object
- 75% were incorrect on the inclination or position of the verb
- 38% were incorrect because of omission of the verb
- 94% were incorrect because of other grammatical failures
- 66% were incorrect because of omission of an article
- 18% were incorrect because of omission of a preposition

Conclusions: Most grammatical mistakes were due to omissions, not only of grammatically less important categories such as articles or prepositions, but also more important parts, such as the verb, object or subject were omitted. The results seem to indicate that the so called ''telegram style'' of HD spoken language is not a conscious strategy to deal with the dysarthria and thus is not a telegram style at all. HD spoken language seems to be more a speaking in fragments. Further research is needed to investigate to what degree the fragmentary HD spoken language is caused by dysarthria or is an effect of language disorders.

Suggestion: Developing a grammatical test to assess HD spoken language.

C.6 WORD LEARNING ABILITIES IN HUNTINGTON'S DISEASE

[1]E Nogueira Teixeira, [1,2,3,4]R de Diego Balaguer, [5]A Mestres-Missé, [2]A Rodríguez-Fornells, [1,3,4,6,7]A-C Bachoud-Lévi. *[1]DEC, Ecole Normale Supérieure, Paris, France; [2]ICREA and Universitat de Barcelona, Barcelona, Spain; [3]INSERM U841, Créteil, France; [4]Université Paris 12, Faculté de Médecine, Créteil, France; [5]Otto-Von-Guericke Universität, Magdeburg, Germany; [6]AP-HP, Groupe Henri-Mondor Albert-Chenevier, Service de Neurologie, Créteil, France; [7]Centre de Référence Maladie de Huntington, Créteil, France*

Background: Recent reports have documented that Huntington's disease (HD) patients show difficulties in those aspects of language requiring rule processing (ie, syntax, morphology), whereas lexical abilities seem to be relatively spared.[1 2] Although these results have been interpreted as a minor involvement of the striatum in lexical processing, this view assumes that words are simple associations between forms and meaning. However, throughout our lifespan we keep on encountering new words in our language and extracting the commonalities of the different contexts in which this new word appears, requiring similar abilities as rule processing.

Aims: Our aim was to study whether HD patients would be impaired in this type of word learning from context.

Methods/Techniques: 12 patients and 18 controls were confronted with a self-paced reading task adapted from Mestres-Missé *et al*[3] including three sentences in each trial having an unknown word at the end of the sentence. After reading the three sentences participants had to guess the meaning of the new word. In the experimental condition the three sentences led to the same meaning (M+), in the control condition the three sentences led to different meanings (M−). In addition, a third condition in which participants had only to give a semantically related word to a real word was included in order to control for the integrity of the semantic system.

Results/Outcome: Although showing comparable performances in semantic abilities to controls, HD patients showed poorer performances in the M+ condition. A significant decrease in reading times was observed in the controls from the first to the third sentence in this condition, whereas the M− condition did not vary. In contrast, HD patients did not show a decrease in reading times through sentences in the M+ condition, always comparable with the M− condition.

Conclusions: These results suggest that language difficulties in HD seem to involve not only rule processing but also lexical processing when this requires the extraction of meaning from different contexts.

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2. **Ullman MT**, Corkin S, Coppola M, *et al*. *J Cogn Neurosci* 1997;**9**:266–76.
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C.7 SENTENCE COMPREHENSION IMPAIRMENT IN HUNTINGTON'S DISEASE

[1,2,3,4]S Sambin, [1,2,3,4]M Teichmann, [3,5]D Sportiche, [3,5]P Schlenker, [3]E Dupoux, [1,2,3,4,6]A-C Bachoud-Lévi. *[1]EQUIPE 1, INSERM U841, Neuropsychologie Interventionnelle, IM3/Paris 12, Créteil, France; [2]Université Paris 12, Créteil, France; [3]Departement d'Etudes Cognitives, Ecole Normale Superieur, Paris, France; [4]Centre de Reference Maladie de Huntington, Créteil, France; [5]UCLA, Los Angeles, California, USA; [6]AP-HP, Hopital Henri Mondor, Service de Neurologie, Creteil, France*

The nature of language impairment in Huntington's disease (HD) is still unclear. Some authors explain it by a co-occurring deficit in non-linguistic functions such as working memory (WM), whereas others propose a disorder of linguistic rule processing. In our study, we disentangled the respective roles of WM and of rule application in sentence comprehension deficits in HD patients, by using two syntactic rules that allow disentangling these two components. We tested WM by manipulating surface distance between the name and its determinant in sentences governed by gender agreement, while syntactic operation is held constant (the girl watches the dog that is green and the girl that watches the dog is green). On the other hand, to test rule application we varied conditions of co-

reference between a noun and a pronoun while holding WM constant: we contrasted sentences in which a linguistic principle (principle C) blocks co-reference (He smiled when Paul entered) and sentences that are ambiguous for co-reference (When he smiled, Paul entered). Fifteen HD patients at stage I of the disease and 15 healthy controls were tested. Results show that patients, likewise controls, have a preference for co-reference in ambiguous sentences; conversely, unlike controls, they accept co-reference even when it is blocked by principle C. An increase of WM in gender agreement sentences has no impact either on controls' or on patients' performance. We show that WM does not affect patients' ability to process syntax, suggesting that sentence comprehension impairment in HD is more likely to rely on linguistic rule deficits than on WM impairment.

C.8 UNDERSTANDING LANGUAGE COMPREHENSION DEFICITS AND SUPPORTING COMMUNICATION IN INDIVIDUALS WITH HUNTINGTON'S DISEASE

L Hartelius, A Fors, A Sahlin, S Ströberg, L Sundin. *Institute of Neuroscience and Physiology, Division of Speech and Language Pathology, University of Gothenburg, Box 452, S-430 40 Göteborg, Sweden*

Background: Individuals with Huntington's disease (HD) are faced with increasing speech as well as cognitive/linguistic communication problems. The overall aim of this ongoing project is to describe the communication disorder and to develop and evaluate different types of strategies to support communication.
Aims: Two studies will be reported and their specific aims were to explore auditory language comprehension in relation to disease progression and evaluate the use of Talking Mats to support communication.
Study 1
Methods: Eighteen individuals in different stages of HD were compared with a control group on general and more complex language tasks. Also, a relative or close friend answered a questionnaire regarding perceived communicative changes.
Results: The results showed significant differences on the general measure of auditory language comprehension, including individuals in early stages compared with their controls, but also significant differences in the ability to understand metaphors, ambiguities and make inferences.
Conclusion: Auditory language comprehension shows great variability within the group of individuals with HD and can be severely affected early on.
Study 2
Methods: Five individuals all in later stages of HD took part in the second study. Three types of interview techniques were compared: unstructured conversation, structured conversation and conversation using Talking Mats (www.talkingmats.com). The interviews were video recorded and evaluated using the protocol Effectiveness Framework of Functional Communication (EFFC).
Results: Talking Mats increased the effectiveness of communication for all five participants.
Conclusion: Talking Mats supports conversation and might also be suitable for individuals with less apparent communicative problems.

C.9 ALTERED AUDITORY SENSORY PROCESSING IN PREMANIFEST HUNTINGTON'S DISEASE: ARE THERE DIFFERENT PHASES IN PREMANIFEST HUNTINGTON'S DISEASE?

[1]C Saft, [2]A Schüttke, [1,2,3]C Beste, [1]J Andrich, [2]B Pfleiderer. *[1]Department of Neurology, Huntington-Center NRW, St Josef Hospital, Ruhr University, Bochum, Germany; [2]Department of Clinical Radiology, University of Münster, Albert-Schweitzer-Strasse 33, 48129 Münster, Germany; [3]Leibniz Research Centre for Working Environment and Human Factors, WHO Collaborating Research Centre, Dortmund, Germany*

Introduction: There are only a few data about the role of striatal-thalamic areas as an analyser in central somatosensory control in Huntington's disease (HD). The aim of this study was to assess auditory sensory processing mechanisms by functional magnetic resonance imaging (fMRI) in patients with premanifest HD.
Methods: 18 premanifest HD and corresponding controls were included. The group was divided into two subgroups close premanifest HD; less than 10 (respectively 14.9) years and far premanifest HD (>10 years), according to their estimated age of disease onset (eAO) using Ranes's and Langbehn's formulae, respectively. Tone perception and processing were characterised by 3T fMRI by employing repeated tone stimulation (three digitally generated pulsed (5 Hz) 800-Hz sine tone blocks (A1–A3)). Statistical analysis was done by SPM2, 2×2×2 mm voxel size and 8 mm kernel. Second level analysis was done by using a t-test, p uncorrected <0.001, minimum cluster size 10 voxels. In addition, individual activation intensities of corresponding areas were determined in defined regions of interest by defining a sphere with a radius of 4 mm around activation maxima.
Results: The close premanifest HD group presented predominantly downregulated processes compared with controls (left BA4 in A1 and right ACC, BA6 and insula in A3), whereas the far premanifest HD group presented with stronger bilateral activation of the right caudatum in A1 and the right globus pallidus, left ACC, BA7, BA46 and right cerebellum in A3. Compared with close premanifest HD activation intensities were significantly higher for the bilateral thalamus and right BA44 in the far premanifest HD group in A1.
Discussion: Our findings seem to reflect an altered activation pattern to auditory stimulation depending on the progression of neuronal dysfunction. They also stress the involvement of the basal ganglia-thalamic circuits in the processing of sensory auditory stimuli. In accordance with other studies using functional techniques we found upregulated processes in our far from eAO group and predominantly downregulated processes in our close premanifest HD group. We suggest that there are different phases of up and downregulation in premanifest HD, depending on the years to eAO.

C.10 INCREASED SUSCEPTIBILITY TO VISUAL ILLUSORY EFFECT IN HUNTINGTON'S DISEASE

AK Ho, JG Smith, JP Harris. *Department of Psychology, University of Reading, Whiteknights Road, Reading RG6 6AL, UK*

Background: An accumulating literature suggests that deficits in visual processing are among the earliest cognitive abnormalities to emerge in patients with Huntington's disease (HD).
Aim: The present study examined the nature of altered visuospatial representations in HD, particularly the degree to which patients are susceptible to illusory effects.
Methods: Nine right-handed patients with HD and 11 right-handed age-matched healthy controls were tested on two self-paced computerised line bisection tasks. The stimuli consisted of plain horizontal lines and lines with bilateral fins whose direction (facing left/right/both) were manipulated to create the Judd illusion effect. In the perceptual bisection task, participants viewed pre-bisected lines on screen and judged whether or not they thought these were accurately bisected. In the motor bisection task, participants used two large buttons to move the bisection mark left or right to their perceived midpoint.
Results: In both perceptual and motor bisection tasks, the HD and control groups made accurate bisection judgements in the baseline (no fins) condition. Both groups also demonstrated significant illusory effects in bisection tasks. However, the magnitude of both left and right-induced visuospatial biases in illusory conditions was significantly greater for HD patients compared with controls, indicating that patients were more susceptible to illusory effects of the flanking visual elements in both perceptual and motor line bisection tasks

Conclusions: The results of this preliminary study suggest that HD patients are more prone to visual distractability compared with controls when performing line bisection under illusory conditions.

C.11 PSEUDO-NEGLECT IN HUNTINGTON'S DISEASE: A RETROSPECTIVE ANALYSIS

M Couette, M-F Boissé, A-C Bachoud-Lévi. *Centre de Référence Maladie de Huntington, Faculté de Médecine, 8 rue du Général Sarrail, 94010 Créteil cedex, France*

Early disorders in visuospatial perception in patients with Huntington's disease (HD) may correspond to a specific phenotype of the disease. Both pseudoneglect and neglect have been described in patients with HD, in a group study and in a single case study, respectively (Ho *et al*, 2003, 2004). Such hemi-attentional troubles in the right visual field are consistent with the time course of the neural degeneration of the disease, damaging first the left striatum evidenced by recent neuroimaging studies. Here, we aimed to confirm the existence of this pseudoneglect profile with a simple visuospatial paper–pencil task (Zazzo's cancellation task) in 20 consecutive unselected patients with 16 controls matched for age and educational level. Participants were instructed to cross out one, two or three small aligned signs covering a full page with a time constraint of 90 s for each page. We analysed their performance by separating the page into two equal parts. We rated the percentage of omissions on both sides (number of omissions/number of targets to cancel). We conducted a two-way analysis of variance with ''target numbers'' (one, two and three signs to cancel) and side (left, right) as within factors. Patients produced more omissions and the task elicited more omissions for the three than two targets condition and even more for the one target than the two targets condition. There was no effect of side but there was an interaction between side and group. The percentage of omissions was more important in the right part in patients only, suggesting a pseudoneglect profile on this rapid and simple paper–pencil task. Further studies are needed to determine what is the relevance of the pseudoneglect disorder as a marker of disease evolution and what is its prognosis value, if any.

C.12 THE POWER OF POSITIVES: EVIDENCE FOR AN OVERALL EMOTIONAL RECOGNITION DEFICIT IN HUNTINGTON'S DISEASE

L Robotham, I Trinkler, D Sauter. *INSERM U841, Créteil, France*

The recognition of emotions of disgust, anger and fear have been shown to be significantly impaired in Huntington's disease (eg, Sprengelmeyer *et al*, 1997, 2006; Gray *et al*, 1997; Milders *et al*, 2003, Montagne *et al*, 2006; Johnson *et al*, 2007; De Gelder *et al*, 2008). The relative impairment of these emotions might have implied a recognition impairment specific to negative emotions. Could the asymmetic recognition deficits be due not to the complexity of the emotion but rather reflect the complexity of the task? In the current study, 15 Huntington's patients and 16 control subjects were presented with negative and positive non-speech emotional vocalisations that were to be identified as anger, fear, sadness, disgust, achievement, pleasure and amusement in a forced-choice paradigm. This experiment more accurately matched the negative emotions with positive emotions in a homogeneous modality. The resulting dually impaired ability of Huntington's patients to identify negative and positive non-speech emotional vocalisations correctly provides evidence for an overall emotional recognition deficit in the disease. These results indicate that previous findings of a specificity in emotional recognition deficits might instead be due to the limitations of the visual modality. Previous experiments may have found an effect of emotional specificy due to the presence of a single positive emotion, happiness, in the midst of multiple negative emotions. In contrast with the previous literature, the study presented here points to a global deficit in the recognition of emotional sounds.

C.13 DISTURBED MOTOR RESONANCE AT THE BASIS OF THE EMOTION RECOGNITION DEFICIT IN HUNTINGTON'S DISEASE? AN EMG INVESTIGATION

[1,2]I Trinkler, [1,2]S Devignevielle, [3]A Achaibou, [1,2]A-C Bachoud-Lévi. *[1]Inserm U841, Equipe 1, Faculté de Médecine Paris XII, 8 rue du Général Sarrail, 94010 Créteil, France; [2]Département d'Etudes Cognitives, ENS, 29 rue d'Ulm, 75005 Paris, France; [3]Laboratory for Neurology and Imaging of Cognition, Department of Neuroscience, University of Geneva, 1 rue Michel-Servet, 1211 Geneva, Switzerland*

Background: Patients with Huntington's disease (HD) have a deficit recognising emotional expressions. Recently, it has become clear that this deficit extends to other modalities and is not specific to disgust (Snowden *et al*, 2008; Johnson *et al*, 2007; Henley *et al*, 2008). In a recent study we established that this recognition deficit comes along with a production and that recognition and production are a highly correlated deficit (Trinkler and Bachoud-Lévi, 2008). This points to a potential role of ''motor resonance'' in emotional recognition, ie, a mechanism for recognising emotional expression in somebody else through an internal motor simulation thereof, which might be impaired in HD.
Aims: We aimed to compare motor resonance and the production of emotional expressions between Huntington's patients and healthy controls using electromyography.
Methods/Techniques: 14 early HD and 14 matched healthy subjects were tested on three conditions of motor production of emotional expressions using electromyography: (1) spontaneous micro-mimickry of emotional expressions as is observed in healthy subjects (Dimberg, 1982); (2) overt imitation of facial expressions; (3) production of facial expressions from emotional words (''anger'', ''disgust'', ''joy''). Measurements were taken repeatedly from three facial regions: zygomatic (active in smiling), corrugator (active in frowning) and nasalis (active in wrinkling the nose in disgust).
Results: HD patients show less and less specific activation of the muscle active in the corresponding emotion in all three conditions. They thus lack automatic facial mimickry and show significantly less imitation and less ability to mime an emotional expression overtly compared with healthy subjects.
Conclusions: The absence of motor resonance for emotional facial expressions in HD might account for their difficulty in recognising emotions in others and may potentially be at the core of an empathy deficit.

C.14 A STUDY OF SOCIAL COGNITION IN HUNTINGTON'S DISEASE USING THEORY OF MIND TASKS

[1,2]V Havet-Thomassin, [3]C Verny, [4]D Bonneau, [3]F Dubas, [1,2]D Le Gall. *[1]Neuropsychology Unit, Department of Neurology, University Hospital of Angers, Angers, France; [2]Laboratory of Psychology (UPRES EA 2646), University of Angers, Angers, France; [3]Department of Neurology, University Hospital of Angers, Angers, France; [4]Department of Genetic, University Hospital of Angers, Angers, France*

Background: Huntington's disease (HD) is a degenerative disorder with predominant involvement of the frontostriatal system. This condition gives rise to altered social and breakdown in interpersonal relationships, although the factors underlying these changes remain poorly defined.
Aims: This study used cognitive and affective theory of mind tasks, respectively, to explore the ability of patients with HD to interpret social situations and their ability to ascribe mental states to others.
Methods: Ten HD patients and 10 healthy volunteers matched by age and educational level were given a non-verbal cognitive theory of mind task assessing the attribution of intentions to others (Brunet *et al*, 2003) and a revised version of the ''Reading the Mind in the Eyes'' Test (Baron-Cohen *et al*, 2001), which is an affective theory of mind task assessing the understanding of other people's mental states from their eyes.
Results: The two measures of theory of mind were indicative of a significant impairment in HD patients.

Conclusions: Our results are consistent with the idea that both cognitive and affective aspects of theory of mind are impaired in HD patients, indicating that cortico-subcortical circuits participate in the mediation of higher social functions. Nevertheless, it would be important to determine precisely the specific role of the striatum in theory of mind performances and the contribution of theory of mind deficits to disorganised behaviour and breakdown in interpersonal relationships in daily life in HD patients, as has been suggested by Snowden *et al* (2003).

C.15 NEUROPSYCHIATRIC ASPECTS OF HUNTINGTON'S DISEASE: COMPARING SELF-REPORT AND CAREGIVER ASSESSMENT OF BEHAVIOURAL CHANGES

J Ullah, M Koppitz, AK Hödl, RM Bonelli, H-P Kapfhammer. *Department of Psychiatry, Medical University Graz, Auenbruggerplatz 31, 8036 Graz, Austria*

Introduction: Huntington's disease (HD) is a hereditary neurodegenerative disorder characterised by a triad of symptoms, namely motor symptoms, cognitive deterioration and psychiatric alterations. Neuropsychiatric abnormalities, such as depression, aggression, anxiety, apathy or sleeping disorders particularly place an enormous emotional burden on patients and their caregivers in their daily life. However, the awareness of these disturbances seems to be impaired in HD patients. The purpose of the current study was to evaluate the difference between patients' and caregivers' perceptions of neuropsychiatric symptoms.
Methods: Thirty patients with HD attending the Department of Psychiatry at the Medical University of Graz and their caregivers participated in the study. The caregivers were administered the Neuropsychiatric Inventory (NPI), a clinical instrument with established validity and reliability. The patients' rating of the neuropsychiatric disturbances perceived was assessed with an adapted version of the NPI (NPIad), which did not evaluate hallucinations and delusions, because of the inability of the affected to perceive them as a pathological change. In addition to that the duration and stage of the disease as well as the Unified Huntington's Disease Rating Scale (UHDRS) scores were documented.
Results: No correlation was found between the caregivers' and the patients' assessment of the neuropsychiatric disturbances and the distress resulting from these. Furthermore, caregivers described a higher frequency and severity of symptoms. The total score of the NPI was significantly correlated with the stage of the disease, the UHDRS cognitive, function and behaviour score and the distress score. Moreover, no correlation was found for the NPIad and the other parameters evaluated.
Conclusions: Patients with HD have a significantly different awareness of neuropsychiatric symptoms in comparison with their caregivers. Disturbances are reported more frequently and severely by the caregivers than by the patients themselves. Impaired perception does not seem to be related to the progression of the disease. Future studies examining larger samples may underline these findings.

C.16 PSYCHIATRY IN HUNTINGTON'S DISEASE

EM Pöschl, RM Bonelli. *Medical University of Graz, Graz, Austria*

At the present time the treatment of Huntington's disease (HD) focuses on the neurological symptoms of the disease such as movement disorders and cognitive impairment. However, in clinical practice, the psychiatric disturbances are just as relevant as the neurological ones, because they often more subjectively impede the daily life of patients. In some cases, psychiatric symptoms such as depression and aggression appear years before the onset of neurological symptoms, so behavioural change may be an early indicator of disease onset. There are no clear results between the correlation of the number of CAG repeats and the age of onset of psychiatric symptoms. We present a systematic review of the major original psychiatric studies in HD, in order of their clinical importance: depression and suicide with a prevalence of 30%, irritability and aggression occur in 60% and 40%, apathy in 57%, psychotic symptoms in up to 12%, anxiety disorders in approximately 28% in the course of disease, obsessive and compulsive symptoms in 20% and mania in approximately 5%.

C.17 HUNTINGTON'S DISEASE RESEMBLING SCHIZOPHRENIA: A CASE REPORT

R Hafenscherer, AK Hödl, HP Kapfhammer, RM Bonelli. *Graz Medical University, Department of Psychiatry, Auenbruggerplatz 31, 8036 Graz, Austria*

We describe the case of a 23-year-old man who was admitted to the Department of Psychiatry of the Graz Medical University. At admission to the clinic he had reportedly suffered from social withdrawal, poor concentration and dysphoria for years. His avolition had caused him to drop out of high school, leaving him without training qualifications and unable to sustain himself socially or to provide minimum self-care. Furthermore, he presented with massive symptoms of thought disorder, mainly disorganised speech and derailment, illogicality and a general poverty of speech. The patient's family history of Huntington's disease (HD) led us to consider an early manifestation of HD as the cause.

The genetic testing revealed 41 repeats of the trinucleotide CAG marking a predisposition for HD. However, a result of 41 CAG repeats makes the onset of HD at this early age highly unlikely as there appears to be a strong negative correlation between the number of CAG repeats and the age at onset of the disease. Moreover, the patient showed no motor symptoms nor pathological eye movements in extensive testing, as used for patients in the early stages of HD.

The treatment with quetiapine and sertralin led to a distinct improvement of the patient's psychiatric symptoms. He became increasingly communicative, organised in thinking and was able to restructure his life. Therefore, we think that the psychiatric symptoms of the patient are most likely unrelated to the patient's predisposition for HD and are probably caused by schizophrenia simplex.

C.18 PAIN IN HUNTINGTON'S DISEASE

C Serpino, C Cormio, V Sciruicchio, P Livera. *Neurological and Psychiatric Sciences Department, University of Bari, Policlinico, Piazza G Cesare 11, 70127 Bari, Italy*

Aims: In the past few years, some research has focused on the effects of motor cortex activation on pain perception and elaboration. Pain is a frequent symptom in early Parkinson's disease, whereas little is known about pain processing in Huntington's disease (HD). The aim of the present study was to examine pain features and nociceptive laser evoked potentials (LEP) in a cohort of HD patients, at an early stage of the disease.
Methods: Twenty HD patients were selected, on the basis of a Mini-Mental State Examination score of 25 or greater, and a clinical onset of 5 years or less. Forty control subjects, age and sex matched, were also examined. The LEP were obtained by five scalp electrodes, positioned at the Fz, Cz, Pz, referred to the nasion. A 0–100 visual analogue scale was employed to rate the stimuli. All subjects were also submitted to the brief pain inventory scale. The dorsum of the right and left hands was stimulated.
Results: Only one patient reported pain of a neuropathic type. All the LEP components appeared bilaterally reduced in amplitude in HD, in respect to controls. The P2 wave amplitude was inversely correlated with the functional capacities score.
Discussion: A pain pathways dysfunction emerged in early HD. The reduced amplitude of all the LEP waves may suggest a

thalamocortical dysfunction linked to the abnormal basal ganglia modulation. This LEP pattern seemed opposite in respect to that previously described in Parkinson's disease patients, who exhibited an LEP amplitude increase, more evident in patients reporting painful symptoms. The facilitation of the motor cortex may reduce nociceptive cortex activation, explaining the rarity of painful symptoms in HD.

C.19 OBJECTIVE MOTOR PHENOTYPE ASSESSMENT OF GAIT AND POSTURE IN HUNTINGTON'S DISEASE: A STUDY IN PROGRESS

H Beckmann, S Rumpf, N Bechtel, HW Lange, R Reilmann. *Huntington Center Münster, University of Münster, UKM, Albert-Schweitzer-Strasse 33, 48129 Münster, Germany*

Background: Patients with Huntington's disease (HD) develop an impairment of balance and gait (Rumpf *et al*, 2007). An objective assessment of gait and balance may serve as a surrogate marker for motor phenotype dysfunction.
Aims: To investigate the sensitivity of different tools, GAITRite mat, force plate, ActiWatches and B&L stride analyser to detect deterioration in motor skills before clinical manifestation, and to assess the correlation of outcome parameters to the severity of HD as assessed by the Unified Huntington's Disease Rating Scale—Total Motor Score (UHDRS—TMS), total functioning capacity and functional assessment scale.
Methods: Presymptomatic and symptomatic HD gene carriers and controls are placed on a force plate (Satel, France) and instructed to stand still with eyes open and closed for 25 s. The stability of centre of mass location is assessed by variables ''SURFACE'' and ''DISTANCE'' reflecting the centre of mass mobility. Subjects are equipped with ActiWatches around both ankles and stride analyser insoles in their socks and instructed to walk down the GAITRite mat in five consecutive conditions: ''normal walking'', ''fast walking'', ''dual task walking'', ''tandem forward/backwards walking'', and ''walking on metronome''. The parameters assessed are velocity, cadence, gait cycle, and quantity of kinesia in counts per 2 s. All subjects are assessed clinically using the UHDRS—TMS, total functioning capacity and functional assessment scale.
Results: Preliminary analysis suggests that all techniques can be applied successfully in assessing motor dysfunction in HD. Differences between symptomatic patients and controls are observed. Statistical analysis comparing presymptomatic gene carriers and controls is currently pending, as are comparisons between the different assessment modalities, but will be available at the time of poster presentation.
Conclusion: The current study will elucidate the feasibility of the use of motor assessment devices, GAITRite mat, force plate, ActiWatches and B&L stride analyser, to provide objective and quantitative readouts of motor phenotype dysfunction in HD.
Funding: RR was supported by a grant from the EHDN.

C.20 GAIT ANALYSIS IN SUBJECTS WITH HUNTINGTON'S DISEASE: IS THERE AN INCREASE IN STRIDE-TO-STRIDE VARIABILITY?

[1]A Olivier, [2]O Beauchet, [1]C Scherer-Gagou, [3]P Allain, [1]F Dubas, [4]D Bonneau, [1]C Verny. *[1]Département de Neurologie, Unité de Neurologie, CHU Angers, 49000 Angers, France; [2]Service de Gérontologie Clinique, CHU Angers, 49000 Angers, France; [3]Département de Neurologie, Unité de Neuropsychologie, CHU Angers, 49000 Angers, France; [4]Service de Génétique Médicale, CHU Angers, 49000 Angers, France*

Introduction: It is currently difficult to specify the passage from the presymptomatic to the early symptomatic stage in patients with Huntington's disease (HD). We hypothesised that a high stride-to-stride variability could be an early clinical marker of the disease. The objective of this study was to compare stride time variability in patients with HD (early and presymptomatic stage) with healthy controls subjects.
Method: Stride time variability in eight patients with HD, five early-stage (40 $\pm$ 8.5 years, 60% women) and three with the presymptomatic form (28.7 $\pm$ 6.7 years, 100% women) and 10 healthy controls (36.1 $\pm$ 7.6 years; 70% women) was measured while walking at normal walking speed using the SMTEC footswitch system.
Results: Stride time variability was 2.4 $\pm$ 0.6% in early-stage HD patients, 1.8 $\pm$ 0.4% in presymptomatic subjects and 1.5 $\pm$ 0.6% in healthy control subjects. There was a trend towards an increase in stride time variability across the three groups ($p = 0.071$). In addition, an asymmetry of stride time variability between the right and left step was shown in the early symptomatic stage of HD compared with the presymptomatic stage (4.6 $\pm$ 3.9 versus 2.0 $\pm$ 1.7; $p = 0.571$).
Conclusion: The results show that stride time variability is higher in subjects with HD compared with healthy controls, with a gradient between the early and presymptomatic stage of HD.

C.21 RELATIONSHIP BETWEEN IMPAIRMENT OF VOLUNTARY MOVEMENTS AND SHORT-TERM MEMORY IN HUNTINGTON'S DISEASE

[1]J Klempir, [1]O Klempiorva, [2]J Stochl, [1]N Spacková, [1]J Roth. *[1]Department of Neurology, 1st Medical Faculty, Charles University, Prague, Czech Republic; [2]Department of Kinanthropology, Charles University, Prague, Czech Republic*

Background: Impairment of voluntary movements and memory precedes the dyskinetic syndrome in Huntington's disease (HD). Working memory and free recall from short-term memory are the most impaired components of memory in HD. These functions strongly depend on attention and executive functions.
Aims: The aim of the study was to find a relationship between impairment of voluntary and involuntary movements and memory deficit in HD.
Methods: Forty patients with genetically confirmed HD in various stages were investigated. The rate of motor involvement was quantified by means of the Unified Huntington's Disease Rating Scale (UHDRS). Voluntary (oculomotor and bradykinesia/fine motor) and involuntary components of UHDRS (rigidity, dystonia and chorea) were evaluated separately. For assessment of memory the auditory verbal learning test and verbal paired associates were used. For estimation of short-term and long-term memory and voluntary components of UHDRS factor scores with Bartlet's factor coefficients were employed. The generalised least squares estimator was used for the corresponding factor analysis.
Results: Voluntary components (bradykinesia/fine motor) were found to be significantly correlated with short-term memory disturbances ($r = -0.412$, $p<0.008$), but not with long-term memory in the auditory verbal learning test and verbal paired associates ($r = -0.286$, $p<0.07$). Involuntary components did not correlate significantly with any part of memory performance.
Conclusions: Correlation of short-term memory performance with voluntary movement impairment together with a lack of correlation of voluntary movement impairment with long-term memory performance indicate mainly decreased potential of the central processing system. Both voluntary movement and short-term memory require more attention and processing speed than the execution of already acquired abilities and recall from long-term memory. Involuntary movements do not load significantly processing capacity. It can be concluded that voluntary movement and short-term memory impairment appear to be more sensitive markers of disease progression than involuntary movements.
Funding: This study was supported by a grant from the Czech Ministry of Health, reg no IGA MZ CR NR8937-4 and from the Czech Ministry of Education, Research Programme MSM0021620849 and MSM 0021620864.

C.22 A NOVEL METHOD OF STIMULUS PRESENTATION FOR EVOKING SACCADES IN HUNTINGTON'S DISEASE PATIENTS WITH CHOREA: PRELIMINARY REPORT

[1]J Ober, [2]E Przedpelska-Ober, [3]D Zielonka, [1]J Dylak, [4]P Kleka. *[1]Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Science, ul Szherezady 132, 60-195 Poznan, Poland; [2]Poznan University of Medical Sciences, Department of Neurology, Poznan, Poland; [3]Poznan University of Medical Sciences, Department of Public Health, Poznan, Poland; [4]Institute of Psychology, Adam Mickiewicz University, Poznan, Poland*

Background: One of the functional biomarkers allowing the precise monitoring of Huntington's disease (HD) development is the distribution of saccadic latency, the time taken to make a saccade to a suddenly displaced visual target. In HD, impairment of cortical, cognitive levels are reflected in characteristic changes in the stochastic distribution of saccadic latency. There is a practical limitation in using this methodology in HD patients because of choreiform head movements.
Method: We use a standard saccadometer, modified so that the stimulus display is attached to the head in close vicinity to the eye (6 cm) and moves exactly with the head. This effectively cancels the vestibulo-ocular reflex response, providing adequate eye stability even when the head is making choreiform movements. The onset of the target is adaptively controlled and tailored to the patient's individual capacity to respond, which facilitates sustaining attention on the task. The horizontal target displacement was 10° randomly to the right or left, with a randomised foreperiod of 1.0–2.0 s.
Results: Saccadic latency distributions of 100 trials recorded by five subjects with proximal display were compared with 100 trials obtained using a conventional saccadometer with a viewing distance of 2.5 m. For four of the subjects, the distributions were significantly different (Kolmogorov–Smirnov, $p<0.001$), as were the medians (t-test on reciprocal medians, $p<0.001$); the remaining subject showed no significant difference in either ($p>0.05$). Overall, the mean latency was 138 ms for the conventional saccadometer and 155 ms for the new version.
Conclusion: This technique is potentially capable of providing constant experimental conditions throughout the whole period of HD progression, and the subjects tested reported viewing the proximal stimuli as more comfortable. However, it must be borne in mind that it cannot be used to make direct comparisons with latency distributions measured with the conventional saccadometer.

C.23 THE TEN EURO NEUROTEST: A SIMPLE, QUANTITATIVE TEST OF DEXTERITY THAT IS USEFUL IN THE FOLLOW-UP OF PRESYMPTOMATIC GENE CARRIERS AND PATIENTS WITH HUNTINGTON'S DISEASE

[1]JPP van Vugt, [1]R Wolkorte, [2]R Bos, [2]CK Jurgens, [3]HW Lange, [3]R Reilmann, [2]RAC Roos. *[1]Medisch Spectrum Twente, PO Box 50000, 7500 KA Enschede, The Netherlands; [2]Leiden University Medical Centre, PO Box 9600, 2300 RC Leiden, The Netherlands; [3]University Hospital of Münster, Domagkstrasse 5, 48149 Münster, Germany*

Background and Aim: We recently introduced the Ten Euro Neurotest (TEN) as a simple, quantified ''bedside'' test for dexterity.[1] In the present study, we validated the TEN in a larger sample of Huntington's disease (HD) patients. Furthermore, we tested whether the TEN can be used as a marker for imminent HD in presymptomatic gene carriers.
Methods: The TEN is performed with 10 coins of one Euro aligned on a straight line in the middle of an A4 paper. The subject is instructed to turn the coins as fast as possible, starting with the most distant coin, and to replace them on the line starting from the top of the paper working downwards. The time is clocked and the accuracy with which the coins are replaced on the line is measured using a ruler. Ninety-two healthy control subjects, 56 patients with manifest HD and 12 presymptomatic gene carriers participated in this study.
Results: Test–retest reliability of the TEN was excellent for ''time'' scores (intraclass correlation coefficient (ICC) for dominant/non-dominant hand in controls 0.91/0.93; in HD patients 0.88/0.94) and good for the ''accuracy'' score (ICC in controls 0.68/0.72; in HD patients 0.71/0.90). Patients performed the TEN slower and less accurately than controls. Dexterity decreased significantly with increasing disease severity (Unified Huntington's Disease Rating Scale motor score, total functional capacity) and genetic disease load (calculated as CAG repeat length ? 35.5 * age).[2] Moreover, the presymptomatic gene carriers already performed worse than the controls.
Conclusions: The TEN is a simple, reliable quantitative tool to measure impaired dexterity in HD. TEN performance is already impaired in presymptomatic gene carriers, suggesting that the TEN can detect imminent HD. TEN scores worsen with increasing disease severity and genetic disease load. These qualities advocate using the TEN in the follow-up of presymptomatic gene carriers and HD patients.

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2. **Penney JB Jr**, Vonsattel JP, MacDonald ME, *et al*. CAG repeat number governs the development rate of pathology in Huntington's disease. *Ann Neurol* 1997;**41**:689–92.

C.24 CAN GAIT INITIATION PARAMETERS BE USEFUL AS EARLY MARKERS OF HUNTINGTON'S DISEASE IN PRESYMPTOMATIC MUTATION CARRIERS?

[1]A Delval, [1]S Bleuse, [2]L Defebvre, [2]K Dujardin, [3]P Krystkowiak. *[1]Department of Clinical Neurophysiology, Lille University Hospital, CNRS UMR 8160, 59037 Lille Cedex, France; [2]Department of Neurology, Lille University Hospital, CNRS UMR 8160, 59037 Lille Cedex, France; [3]Department of Neurology, Amiens University Hospital, CNRS UMR 8160, 80054 Amiens Cedex, France*

Objective: To quantify gait initiation disturbances in presymptomatic Huntington's disease (HD) patients.
Background: Gait initiation combines preparation and execution of the first step. Interaction between motor and cognitive aspects of preparation and execution of movement can be studied using a paradigm of gait initiation with and without external cueing.
Methods: 10 presymptomatic mutation carriers (PMC), 10 symptomatic HD subjects and 10 age-matched controls were recorded. They had to initiate gait with and without an external beep.
Results: PMC demonstrated decreased first step speed ($p<0.05$) and duration ($p<0.05$) compared with controls in both conditions. PMC presented a shorter amplitude of the postural adjustments in PMC compared with controls. These impairments were more pronounced in HD subjects.
Conclusions: Preparation and execution of first step are impaired in PMC in both self-triggered and externally cued conditions. Temporal parameters of step execution (step duration), but also spatial parameters of postural adjustments preceding first step (backward shift of the centre of pressure) could be considered as early markers of the disease.

C.25 IMPAIRMENTS OF POSTURAL CONTROL IN PATIENT'S WITH HUNTINGTON'S DISEASE WHILE SITTING: A NEW MOTOR PHENOTYPE BIOMARKER?

[1]S Rumpf, [1]H Beckmann, [1]S Bohlen, [1]N Bechtel, [2]P Kraus, [1]H Lange, [1]R Reilmann. *[1]Huntington Center Münster, University of Münster, UKM, Albert-Schweitzer-Strasse 33, 48129 Münster, Germany; [2]Huntington Center NRW, University of Bochum, Stadionring 23b, 44791 Bochum, Germany*

Background: Patients with Huntington's disease (HD) develop a progressive impairment of stability of stance and walking (Rumpf *et al*, 2007), frequently resulting in falls and injuries. Objective

assessment of postural control in HD may be helpful to assess the risk of injury and serve as a surrogate for motor phenotype dysfunction.
Aim: To investigate whether patients with HD exhibit impairments in the control of postural stability while sitting with or without the availability of visual feedback and to assess whether these measures correlate with the severity of disease as assessed clinically by the the Unified Huntington's Disease Rating Scale—Total Motor Score (UHDRS—TMS).
Method: HD patients (n = 15) and controls (n = 13) were seated on a force plate (Satel, France) with eyes open and closed for 25 s. Subjects were instructed to sit still. Stability of centre of mass (COM) location was assessed by the variables SURFACE and DISTANCE reflecting COM mobility. Data were stored and analysed using a data acquisition system. All subjects were assessed clinically using the UHDRS—TMS. Non-parametric statistics were performed to compare patients and controls (Mann–Whitney test) and to assess dependent variables (Wilcoxon test) using SPSS 15.0. Correlation analysis was performed using non-parametric Spearman correlations.
Results: Both measures SURFACE and DISTANCE were significantly increased in HD compared with controls ($p<0.001$ for all conditions except DISTANCE for eyes closed with $p = 0.002$). In HD SURFACE ($r = 0.74$, $p = 0.004$ eyes open; $r = 0.64$, $p = 0.018$ eyes closed) and DISTANCE ($r = 0.78$, $p = 0.001$ eyes open; $r = 0.63$, $p = 0.019$ eyes closed) were correlated with the severity of the disease as assessed in the UHDRS—TMS.
Conclusion: Assessment of stability of sitting using a force plate provides objective and quantitative readouts of motor phenotype dysfunction in HD. The measures SURFACE and DISTANCE of COM dyslocation were correlated with the severity of motor phenotype (UHDRS—TMS). A possible use of these measures as surrogate markers for trials in HD warrants further exploration.

C.26 A SENSITIVITY COMPARISON OF CLINICAL TESTS OF POSTURAL INSTABILITY IN PATIENTS WITH HUNTINGTON'S DISEASE

[1]H Brozova, [1]M Kucharik, [2]J Stochl, [1]J Klempir, [1]E Ruzicka, [1]J Roth. *[1]Department of Neurology, 1st Medical Faculty, Charles University, Prague, Czech Republic; [2]Department of Kinanthropology, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic*

Objective: To determine which clinical tests of postural instability (PI) in patients with Huntington's disease (HD) are most sensitive and which symptoms are associated with PI.
Background: Balance disorder is one of the common symptoms of HD and can occur in early stages of the disease. PI causes falls and resulting injuries and has a large impact on patient independence.
Methods: We examined 20 HD patients (11 women, nine men) with a mean age of 50.4 years (SD 12.1), a mean disease duration of 6.2 years (SD 2.5) and a mean number of CAG triplets of 45.5 (SD 4.6). Patients were evaluated using the Unified Huntington's Disease Rating Scale (UHDRS), Mini-Mental State Examination (MMSE) and six clinical tests of PI (pull test, push and release test, stance with feet close together, one limb stance, tandem stance and tandem gait). Results of the six PI tests were used in computing a factor score representing the level of instability in each patient. The above tests were compared with a questionnaire we developed regarding PI disorders and falls that was given caregivers and patients independently.
Results: PI was found in 16 out of 20 patients. The clinicians examination correlated more with the caregivers' response to the questionnaire ($r = 0.78$) than with the patients' response ($r = 0.51$). In addition, there is a high correlation between the validity of patients' response with MMSE score ($r = -0.87$). Factor analysis showed that the stance with feet close together and tandem gait best correlated with the factor of instability. PI was found to be correlated with MMSE, the subscore of independence scale and of the functional assessment of UHDRS; in particular there was a high correlation with the Luria test. In addition, the push and release test was not able to be completed in six patients because of lack of cooperation due to cognitive impairment.
Conclusions: The tests of stance with feet close together and tandem gait were best able to predict falls. The push and release test is not a suitable test for HD patients because of the high prevalence of cognitive difficulties. The strong correlations of PI with MMSE score and the Luria test suggest that PI in patients with HD is related to cognitive impairment.

C.27 ANALYSIS OF FALLS OF PATIENTS IN THE LATER STAGES OF HUNTINGTON'S DISEASE IN A SPECIALIST UNIT

S Duport, A Worsley, R Twiston-Davies, L Broadhurst, C Hopkins, B Daveson, S Soeterik, S Crawford, E Gale, A Scott, M Baker, H Finch, DM Salanio, J Cabungcal, L Dauya, R Ojuluwayo. *The Royal Hospital for Neurodisability, Putney, London, UK*

Background: The Royal Hospital for Neurodisability provides assessment, rehabilitation, treatment and long-term placements for people with HD. The HD service is provided over three different geographical areas, each suited to the differing stages of the disease from the middle to the late stage.
Aim: This project aims at giving an overview of falls experienced by people with HD at the Royal Hospital for Neurodisability to highlight the pattern of fall activity with this population in our environment and to identify ways to reduce falls across the service and work towards local standards of practice.
Method: The multidisciplinary group has reviewed retrospectively the incidence of falls reported over the past 2 years. The dataset was composed of the name of the patient, date and time of accident, severity of the falls and a brief description of the accident.
Results: 101 falls were reported over the 2 years. Ninety per cent of the falls were experienced by mobile patients, ie, middle stage of the disease and falls were marginal in the later stage of the disease (only 10%). 97% of the falls resulted in either no injury or just a bruise, two falls resulted in a cut and only one required A&E admission. The head was the main site of impact. Falls mainly occurred when patients where attempting to mobilise. The average number of falls per patient was five (with a range of 0–22). The distribution of falls per time of the day showed two peaks: one around 10:00 hours and one around 16:30 hours.
Conclusions: Falls are a real risk for patients with HD who are mobile. However, with a good risk assessment system, an adapted environment and the appropriate standards of care the outcome of falls can be minimised and the impact on patient independence limited. It is a difficult balance to strike between supporting the independence of the patient and preventing falls over the trajectory of the illness.

C.28 THE INFLUENCE OF PSYCHOPHARMACOLOGICAL MEDICATION ON URODYNAMICS IN PATIENTS WITH HUNTINGTON'S DISEASE

MW Koppitz, KM Reisinger, AK Hödl, H-P Kapfhammer, RM Bonelli. *Medical University Graz, Auenbruggerplatz 31, 8036 Graz, Austria*

Introduction: Huntington's disease (HD) is an incurable illness with dominant heredity characterised by neurodegeneration. Between the ages of 35 and 45 years the first clinical symptoms (choreatic movements, psychiatric problems such as speech disorder, depression or dementia) appear. Patients with HD need a variety of medications in order to ease the symptoms. In our study we investigated the influence of antidepressants, benzodiazepines and neuroleptics on the urodynamic parameters in patients with HD.

Method: We included 37 patients with HD (17 women and 20 men, age 41.93 ± 7.99 years) in our study. The following urodynamic parameters were examined: maximum flow rate, voided volume, flow time, strangury volume, bladder capacity, number of detrusor contractions, intensity of detrusor contractions, frequency of micturition, fill rate, premicturition pressure, intravesicular pressure, compliance and detrusor pressure. Normal distribution was checked using the Kolmogorov–Smirnov test. Group differences were checked with the t-test or Mann–Witney U-test for significance.
Results: Patients treated with neuroleptics show a significantly lower intravesicular pressure (25.14 cm H_2O; $p = 0.026$) compared with the neuroleptic-free group (47.61 cm H_2O). Other urodynamic parameters are not influenced by neuroleptics. We did not find any significant effect for antidepressants and benzodiazepines on function of the bladder. Disease progression was included as a covariate in our analysis.
Discussion: The aim of our study was to investigate the influence of neuroleptics, antidepressants and benzodiazepines, often used in the symptomatic treatment of HD, on bladder function. Antidepressants and benzodiazepines do not show any effect on examined urodynamic parameters. Only patients with neuroleptics show, compared with the non-neuroleptics group, a significant reduction of intravesicular pressure. Although the decrease is rather strong, there seems to be no clinical effect. The lowering of intravesicular pressure could be explained by the α-antagonising side effect of low potency neuroleptics reducing bladder resistance. Summing up bladder function in patients with HD is not influenced by psychopharmacological medication according to our data.

C.29 DYSPHAGIA IN HUNTINGTON'S DISEASE: A COURSE ANALYSIS

[1]KM Reisinger, [2]W Habermann, [1]AK Hödl, [1]M Magnet, [1]RM Bonelli. *[1]University Clinic of Psychiatry, LKH, Graz, Austria; [2]University Clinic of HNO, LKH, Graz, Austria*

Introduction: In the terminal stage of Huntington's Disease (HD) patients often die of the consequences of aspiration pneumonia. In the literature there are no studies on the course of dysphagia in HD.
Methods: We used a prospective blind cohort study for our evaluation.The analysis of the video fluoroscopy was done by two investigators by using defined criteria. For statistical analysis we used the Spearman correlation. We investigated 73 genetically confirmed HD patients in different stages of illness.
Results: We found significant correlation at stage of HD and drooling, building of the bolus, pathological deglutition reflex, leaking and passage of the bolus, days of illness and building of the bolus, oral control of the bolus, pathological deglutition reflex, leaking and penetration.
Conclusion: Our results show that in patients with HD the laryngeal and oesophageal phase of the act of swallowing are not disturbed for a long time by HD. The oral phase is noticeably affected earlier.

C.30 WEIGHT LOSS IN HUNTINGTON'S DISEASE IS RELATED TO THE NUMBER OF CAG REPEATS

[1]NA Aziz, [2]JMM van der Burg, [3]GB Landwehrmeyer, [2]P Brundin, [4]T Stijnen, [1]RAC Roos. *[1]Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands; [2]Neuronal Survival Unit, Department of Experimental Medical Science, Wallenberg Neuroscience Center, Lund University, Lund, Sweden; [3]Department of Neurology, Ulm University, Ulm, Germany; [4]Department of Medical Statistics, Leiden University Medical Center, Leiden, The Netherlands*

Background: Huntington's disease (HD) is a hereditary neurodegenerative disorder caused by an expanded number of CAG repeats in the huntingtin gene. A hallmark of HD is unintended weight loss, the cause of which is unknown.
Aims: In order to elucidate the underlying mechanisms of weight loss in HD, we studied its relation to other disease characteristics including motor, cognitive and behavioural disturbances and CAG repeat number.
Methods: In 517 early-stage HD patients, we applied mixed-effects model analyses to correlate weight changes over 3 years to CAG repeat number and various components of the Unified Huntington's Disease Rating Scale (UHDRS). We also assessed the relation between CAG repeat number and body weight and caloric intake in the R6/2 mouse model of HD.
Results: In HD patients mean body mass index decreased by −0.15 units per year ($p<0.001$). However, no single UHDRS component, including motor, cognitive and behavioural scores, was independently associated with the rate of weight loss. Conversely, each unit increase in CAG repeat length was associated with a faster rate of weight loss in HD patients. In R6/2 mice, larger CAG repeat lengths were also accompanied by a lower body weight, whereas caloric intake was higher in mice with larger repeat lengths.
Conclusions: Weight loss in HD is directly linked to CAG repeat length and is likely to result from a hypermetabolic state. Other signs and symptoms of HD are unlikely to contribute to weight loss in early disease stages. Elucidation of the responsible mechanisms could lead to effective energy-based therapeutics.

C.31 ASSESSMENT OF ADVANCED HUNTINGTON'S DISEASE PATIENTS WITH THE LATE-UHDRS: A PILOT STUDY

[1,2]K Youssov, [3]RAC Roos, [1,2,4]A-C Bachoud-Levi. *[1]Centre de Référence Maladie de Huntington, CHU Henri Mondor, 94010 Créteil, France; [2]INSERM U841, Créteil, France; [3]Department of Neurology, LUMC, Leiden, The Netherlands; [4]Département d'Etudes Cognitives, Ecole Normale Supérieure, Paris, France*

Background: The Unified Huntington's Disease Rating Scale (UHDRS) has confirmed efficacy in Huntington's disease (HD) assessment, and is used worldwide for clinical studies. However, it appeared substandard for late-stage changes in rating over time. The lack of efficient measures in advanced patients thus excludes them from potential therapeutic trials.
Aims: We have designed the Late-UHDRS scale, inspired by the regular UHDRS, in order to fill out specific clinical changes in advanced HD. It aims to overcome the limitations of examination due to the patient's communication disorders.
Methods: It provides four scores in the motor, vegetative, cognitive and behavioural domains, contains 40 items and takes less than 30 minutes to complete. Patients were selected with a total functional capacity less than 5 and assessed in Créteil and Leiden with both this scale and the regular UHDRS.
Results: 46 patients (25 in Créteil, 21 in Leiden) were assessed, 13 cross-sectionally and 33 longitudinally with a mean 10.9 months interval (SD 4.8). We assessed the internal consistency and longitudinal changes, compared with the regular UHDRS and the interrater reliability.
Conclusions: Altogether, compared with the regular UHDRS, the Late-UHDRS seems more efficient for longitudinal assessment in advanced HD patients and is easier to assess independently from the presence of a caregiver at the examination.

C.32 THE BEHAVIOUR OBSERVATION SCALE HUNTINGTON'S DISEASE: LONGITUDINAL VALIDATION

[1,2]R Timman, [3]H Claus, [1]R Roos, [1,2]A Tibben. *[1]Department of Neurology, Clinical Genetics, Leiden University Medical Centre, PO Box 9600, NL-2300 RC Leiden, The Netherlands; [2]Centre of Human and Clinical Genetics, Leiden University Medical Centre, PO Box 9600, NL-2300 RC Leiden, The Netherlands; [3]Nursing Home Overduin, Topaz, PO Box 525, NL-2220 AM Katwijk, The Netherlands*

Background: In nursing homes for patients with Huntington's Disease there is a need for an observation instrument quickly and easily to assess the patient's behavioural pattern. The Behaviour

Observation Scale Huntington (BOSH) is a promising instrument for this purpose, but its structure and characteristics have been studied on a minimal (cross-sectional) sample and a limited number of administrations. The first analyses have yielded three components: deterioration of activities of daily living, social-cognitive deterioration and rigidity-aggression. More data are expected to reveal more and more precise components. Clinical observation has pointed to possible components, such as fractiousness, cognitive functioning, inflexibility and eating and drinking capacities.

Aims: To determine the component structure of the BOSH more precisely. To describe the course of disease in terms of the components and to discriminate groups of patients on behavioural patterns.

Methods: In the period between 2000 and 2008 the BOSH has been administered every 6 months for a total of more than 100 patients in the nursing home Overduin in Katwijk, The Netherlands.

Statistical Methods: Three-mode principal component analysis will be used for determining the principle components. Regression mixed modelling in SAS (PROC MIXED) will be used to determine the time course of the subscales. Discriminant analyses will be performed for determining possible subgroups.

Results: The first preliminary results on principle component structure and course of the disease will be presented.

C.33 BENIGN HEREDITARY CHOREA: CLINICAL AND NEUROIMAGING DATA FROM A FAMILY WITH NEW MUTATION OF THE THYROID TRANSCRIPTION FACTOR GENE

[1]L Di Maio, [1]E Zampella, [1]M Ferrara, [2]S Pappatà, [1]P Macchia, [1]G De Michele. *[1]University Federico II, Via Pansini 5, Napoli, Italy; [2]IBB-CNR, Via Pansini 5, Napoli, Italy*

Objective: To describe clinical and morph-functional changes in a pedigree with chorea due to a novel thyroid transcription factor 1 (TITF-1) mutation.

Background: TITF-1 mutations have recently been associated with benign hereditary chorea, an autosomal dominant disorder, characterised by chorea and possible hypothyroidism and respiratory alterations.

Design/Methods: A 23-year-old woman presented with involuntary choreiform movements, since she was 8 years old. Her father, a 54-year-old man, had slight, sporadic, hyperkinesias since childhood. The proband's son had neonatal respiratory distress, pyelectasis, congenital hypothyroidism, psychomotor developmental delay and recently developed slight, sporadic limb hyperkinesias. We studied the patients extensively, we sequenced the entire TITF-1 gene and performed TITF-1 functional analysis.

Results: Subclinical hypothyroidism was found in the proband and in the father. Magnetic resonance imaging evidenced ventricular dilatation in both patients. Positron emission tomography was normal in the proband, but showed caudate and left temporo-parieto-occipital hypometabolism in the father. Neuropsychological evaluation showed long-term verbal memory deficit and mild intelligence test impairment in the proband, whereas mainly short-term memory deficit was shown in the father. In all the three affected members of the family, we found a heterozygous change in the TITF-1 gene, not previously described, from cytosine to adenine in the second base of the triplet encoding for the amino acid at position 145. The mutation is responsible for a change from serine to a stop codon (S145X). A functional analysis shows that the mutated TITF-1 is not binding DNA, nor activating the canonical thyroid target gene promoter or interfering with the ability of wild-type TITF-1 to activate the transcription and it is mostly in the cytoplasma.

Conclusions/Relevance: Up to now, 19 different mutations of TITF-1 have been found in several families affected by benign hereditary chorea. We report a novel mutation in the exon 2 of the TITF-1 gene in a family in which the phenotype is heterogeneous and more severe in new generations.