

The capacity of attention and simultaneous perception of objects: A group study of Huntington's disease patients

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Abstract

Using a whole report-paradigm based on [Bundesen, C. (1990). A theory of visual attention. *Psychological Review*, 97, 523–547; Bundesen, C. (1998). A computational theory of visual attention. *Philosophical Transactions of the Royal Society of London B, Biological Sciences*, 353, 1271–1281] theory of visual attention (TVA), [Finke, K., Bublak, P., Dose, M., Müller, H. J., & Schneider, W. X. (2006). Parameter-based assessment of spatial and non-spatial attentional deficits in Huntington's disease. *Brain*, 129, 1137–1151] demonstrated profound reductions in perceptual processing speed and visual working memory (WM) storage capacity in Huntington's disease (HD) patients. A comparably severe impairment of visual processing capacity has previously been reported for two simultanagnosia patients [Duncan, J., Bundesen, C., Olson, A., Humphreys, G., Ward, R., Kyllingsbaek, S., van Raamsdonk, M., Rorden, C., & Chavda, S. (2003). Attentional functions in dorsal and ventral simultanagnosia. *Cognitive Neuropsychology*, 20, 675–702]. To investigate whether such a deficit does also prevail in HD, the simultaneous perception of visual objects was tested in 10 HD patients under free viewing conditions and without time constraints. Objects were presented under four different conditions: (i) single, (ii) multiple adjacent, (iii) multiple embedded, and (iv) multiple overlapping. The dependent measure was the percentage of identification failures. Performance was compared to that of 15 healthy subjects matched for age, education, gender and general mental ability. For HD patients, the percentage of errors in the various testing conditions was examined for correlations with the TVA parameters of visuo-perceptual processing speed and WM storage capacity. These parameters were estimated using verbal whole report of briefly presented letters. TVA permits the two parameters to be estimated mathematically independently and relatively unaffected by any motor deficits present in HD. The identification error rate was substantially increased in HD patients, compared to control subjects, in the overlapping-figures subtest. This deficit was significantly and negatively correlated with processing speed, whereas there was no correlation with WM storage capacity. These results demonstrate the presence of deficits in simultaneous perception in HD, related to a severe reduction in perceptual processing speed. The results are discussed with respect to a dopamine mediated decline of cortical cholinergic activation, diminishing the number of visual objects that can be simultaneously represented within the visual processing system.

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1. Introduction

Huntington's disease (HD) is an autosomal dominant inherited disorder related to an expansion of the trinucleotide repeat

CAG in the HD gene (HDCRG, 1993). HD is characterized by a progressive atrophy of subcortical structures, especially in the nucleus caudatus and putamen, giving rise to a progressive disruption of functionally segregated fronto-striatal loops (Andrews & Brooks, 1998; Chow & Cummings, 1999). A number of recent studies have also indicated an early cortical involvement (Andrews & Brooks, 1998; Ho et al., 2004; Thieben et al., 2002), especially in bilateral parietal regions. Early cognitive symptoms associated with the neuropathology of HD include impairments in visual perception, attention and

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executive functions (Tost, Wendt, Schmitt, Heinz, & Braus, 2004; Watkins et al., 2000).

The question whether HD related cognitive impairment reflects striatal or cortical degeneration remains controversial. However, data from asymptomatic gene carriers clearly suggest a prominent role for the striatum in generating cognitive deficits early during the disease. An important component in this regard is the decline in dopaminergic neurotransmission within cortico–striatal pathways (Bäckman & Farde, 2001; Lawrence et al., 1998) which is known as a key regulatory system for modulating attention, working memory, and executive functions (Nieoullon, 2002). In HD, neurodegeneration preferentially affects medium-sized GABAergic spiny neurons, the predominant neuronal population in the striatum (Charvin, Vanhoutte, Pagès, Borrelli, & Caboche, 2005; Graveland, Williams, & DiFiglia, 1985; Goto, Hirona, & Rojas-Corona, 1989). These neurons, which are mainly projection neurons innervating the substantia nigra and globus pallidus, bear a high density of post-synaptic D1 and D2 receptors. During HD, there is a decrease of D1 and the D2 receptor density (Ginovart et al., 1997; Hägglund et al., 1987) which is correlated with cognitive deficits, for example in tasks, in which the rate at which information can be processed or retrieved is a critical component (Bäckman, Robins-Wahlin, Lundin, Ginovart, & Farde, 1997). After onset of the first symptoms, and as the disease further progresses, a marked degeneration in thalamic and neocortical regions can be found (Rosas et al., 2005). At this stage, cognitive deficits clearly are the result of a cortico–striato–thalamic system that is affected at multiple sites, and disentangling the differential contribution of striatal and cortical areas is difficult.

Recently, we have found symptomatic patients with HD to suffer from a severe progressive reduction in visual processing speed and visual working memory (WM) storage capacity (Finke, Bublak, Dose, Müller, & Schneider, 2006). The whole report-paradigm used in this study (Duncan et al., 1999; Bublak et al., 2005; Finke et al., 2005), which requires non-speeded verbal (rather than speeded manual) responses, permitted the two attentional components to be assessed mathematically independently and not confounded by motor deficits such as bradykinesia prevalent in HD (Agostino, Berardelli, Formica, Acconero, & Manfredi, 1992; Sánchez-Pernaute et al., 2000).

HD patients' perceptual slowing in both visual hemi-fields was comparable in magnitude to that observed in patients with simultanagnosia by Duncan and colleagues (2003) who used a similar assessment procedure. Simultanagnosia is a core symptom of Bálint's syndrome which has been reported to occur in different forms of neurodegenerative disorder (e.g., Benson, Davis, & Snyder, 1988; Huberle & Karnath, 2006; Mendez, Turner, Gilmore, Remler, & Tomsak, 1990; Rizzo & Vecera, 2002; Tang-Wai et al., 2004). As a result patients with HD might also exhibit a similar impairment. Yet, to our knowledge, there have been no investigations of this question to date. Given that studies assessing cognitive performance deficits in HD patients have usually employed relatively complex stimulus material, it would be important to know whether these patients are generally able to perceive multiple (i.e., simultaneously presented) objects in visual displays.

Patients with simultanagnosia suffer from a profound failure to report all of several objects presented simultaneously, although recognition of individual objects is usually intact (Coslett & Saffran, 1991; Holmes, 1918; Wolpert, 1924). Wolpert (1924) defined simultanagnosia as the inability to interpret the whole of a scene despite a preserved ability to apprehend the individual parts. Even if visual fields and acuity are intact, these patients, when presented with multiple-object displays, are unable to perceive all of the objects, reporting only one in extreme cases. Luria (1959) observed that, if presented with two overlapping triangles of different colours forming a 'star of David', simultanagnosia patients could often report only one of the triangles. Since the objects are presented at the same spatial position in this case, the deficit cannot simply be explained in terms of impaired shifting of spatial attention as the core problem.

Impairments of simultaneous perception, be it space-based (Baylis, Simon, Baylis, & Rorden, 2002) or object-based (Duncan et al., 2003), have been grossly characterized as an attentional deficit (e.g., Rizzo & Hurtig, 1987; Rizzo & Robin, 1990). However, especially with respect to object-based impairment, the precise neuro-cognitive mechanisms contributing to the observed deficit are not clearly understood. According to one influential account, it represents a restriction in object-based attention, further increasing the limits that also normally constrain the ability to identify several stimuli in parallel (Duncan et al., 2003). Interestingly, this interpretation is quite similar to the view already put forward by Ranschburg and Schill (1932). They argued that the quantity of "attentional energy" available to perceive shapes is decreased, with the perception of only one or two shapes exhausting the available energy, thus restricting the number of shapes that can be perceived simultaneously.

A modern and more explicit account of the available capacity of visual attention has been proposed in Bundesen's "theory of visual attention" (TVA; Bundesen, Habekost, & Kyllingsbæk, 2005). In TVA, two capacity aspects of the visual processing system are considered: perceptual processing speed and visual working memory (WM) storage capacity. Reductions in both aspects could contribute independently to failures in reporting multiple visual objects in a display. In fact, some authors have proposed that the crucial impairment in simultanagnosia is a reduction in visual WM storage capacity (Coslett & Saffran, 1991), while others have argued that it is a reduction in perceptual processing speed (Kinsbourne & Warrington, 1962).

There is an abundant literature on the storage capacity of visual WM (e.g. Delvenne & Bruyer, 2004). Evidence in favour of reduced WM storage capacity comes from Coslett and Saffran (1991) and Pavese, Coslett, Saffran, Buxbaum, and Lie (2002). Pavese et al. (2002) reported that the ability of a patient with simultanagnosia to name pairs of line drawings improved substantially when the two drawings were presented singly in alternation or when both drawings were presented together initially, but one was removed after a certain period of time. The authors proposed that the patient was unable to "unlock" attention from an attended object; only when attention was "released" by the offset of this object could be shifted to the other one. As the underlying cause, Pavese et al. assumed a weakening

of the visual storage buffer, which gives rise to failures in combining (“binding”) shape and position properties of more than one object and, therefore, in establishing and maintaining more than one “object file” (see Friedman-Hill, Robertson, & Treisman, 1995, for a similar account; for a discussion of the binding problem in visual WM, see e.g. Delvenne & Bruyer, 2006). Consistent with this view, Coslett and Saffran (1991) reported a patient who was able to name briefly presented four-letter words (requiring binding capacity for a single word object file only), but was unable to report four letters forming a non-word string (requiring capacity for four object files). Thus, a severely reduced WM storage capacity (to a single item in the extreme) might leave the processing of one object normal, but render the processing and report of any additional object in the display impossible. This could explain why ‘stickiness’ of perception occurs in simultanagnosia, indicative of ‘hyperattention’ to a single object (Friedman-Hill et al., 1995) and an inability to shift attention between objects (Coslett & Saffran, 1991). However, Huberle and Karnath (2006) reported patients with simultanagnosia to show improved recognition for the global level of Navon-type hierarchical letter stimuli (i.e., for the larger, global, letter which is formed by smaller, local, letter elements; Navon, 1977), with greater numbers of elements and smaller inter-element spacing at the local level. This finding questions limitations of WM storage capacity as being the (sole) cause of simultanagnosia.

Evidence for an account in terms of perceptual processing speed, on the other hand, has been provided by Duncan et al. (2003). Using a TVA whole report-paradigm in two patients with dorsal and ventral simultanagnosia, Duncan et al. found the clinical symptoms of simultanagnosia to be related only to a slowed visuo-perceptual processing speed (but not to a reduced WM storage capacity). From this, they argued that, for everyday visual scenes with multiple elements competing to be processed, a massive reduction in processing speed may cause perceptual failure for all but the most prominent element. A general slowing of visuo-perceptual processing speed would imply that identification is slowed even for single-element displays. Consistent with this, there have been reports that simultanagnosia patients can show abnormalities also in single-element processing, when stimuli are presented serially, though in rapid succession (Friedman & Alexander, 1984; Kinsbourne & Warrington, 1962; Levine & Calvanio, 1978). A number of authors therefore suggested that a ‘general weakening’ of visual traces (Luria, 1959) or visual representations (Bálint, 1909) slows even the perception of single objects, though disproportionately affecting the perception of multiple objects.

In a review discussing potential mechanisms underlying simultanagnosia, Rizzo and Vecera (2002) have recently proposed that future work should specifically consider visual WM storage and attentional functions to gain a clearer understanding of the syndrome. Furthermore, the authors remarked that, since the disorder is relatively rare and difficult to assess using standard clinical tools, the literature is dominated by case reports. Although the single-case approach has undoubtedly provided valuable insights into the normal mechanisms of vision and attention, it entails a number of difficulties: first, less strik-

ing cases are far less likely to be reported than ‘interesting’ abnormalities, although the latter might not be representative with regard to the ‘typical’ underlying mechanisms of the disorder. Second, different authors used a variety of assessment tools and conceptual frameworks of selective attention to interpret patients’ performance, which are difficult to compare with each other. Group studies, by contrast, permit inter-individually varying degrees of severity of ‘simultanagnosic’ deficits to be correlated with reductions in attentional capacity, thereby allowing for a more systematic study of the relationship between the clinically observable behaviour and the underlying attentional mechanisms.

The starting point for the present study was that patients with HD examined by Finke et al. (2006) exhibited similarities in terms of reductions in both processing speed and WM storage capacity with the two simultanagnosia patients examined by Duncan et al. (2003). We thought this to suggest that HD patients might show impaired simultaneous perception in free-viewing conditions that usually cause difficulties in patients with simultanagnosia. Consequently, the present study was designed to examine this question in HD patients using tests with unlimited stimulus exposure and furthermore, we asked whether this impairment would be related to reductions in visual WM storage capacity and/or perceptual processing speed.

In order to examine impairments in the (simultaneous) perception of multiple objects, we used a test procedure with line drawings presented either (i) alone, (ii) adjacent to each other, (iii) in an embedded, or (iv) in an overlapping arrangement. Especially the latter arrangement was expected to reveal a deficit in disentangling overlapping contours—a classic sign of simultanagnosia (e.g., Laeng, Kosslyn, Caviness, & Bates, 1999; Valenza, Murray, Ptak, & Vuilleumier, 2004).

In order to test for impairments in WM storage capacity and processing speed, we used a procedure based on Bundesen’s (1990, 1998) TVA. In TVA, selection of an object is synonymous with its encoding into a visual working memory store with limited capacity. The selection probability is determined (a) by an object’s processing rate v , and (b) by the capacity of the working memory store (if the store is filled, the selection process terminates). Within the computational framework of TVA, processing speed and WM storage capacity are basic attentional parameters (C and K , respectively) that can be derived from a subject’s performance in a whole-report task. In this paradigm, subjects are briefly presented with letter arrays, and their ability to perceive and report multiple letter stimuli is assessed as a function of the array exposure duration. As described in the method section, the two attentional parameters can be estimated separately and independently, based on the resulting performance. Quantitative estimates are thus derived of the maximum number of objects that can be maintained simultaneously in the visual WM store (parameter K) and of the number of objects that can be processed in parallel per second (parameter C). Since severe reductions in processing speed and visual WM storage capacity in HD patients have already been documented, the present study focused on the relationship between the degree of these deficits and the severity of the impairment in reporting simultaneously presented stimuli.

2. Method

2.1. Subjects

Ten symptomatic patients (seven male, three female) with the diagnosis of HD were included in the study. Informed consent according to the Declaration of Helsinki II was obtained from all patients or, respectively, their legal representatives, and the study was formally approved by the ethics committee of the University of Munich. All patients were in-patients of the Huntington-center South, Taufkirchen, Germany, a special neuro-psychiatric ward for HD patients. They all displayed motor symptoms, including dyskinesias, dysarthria, and slowed saccadic eye movements, but were able to maintain fixation, understand verbal instructions, and concentrate on the experimental tasks for about 45 min (the criteria for inclusion in the study). All patients had normal or corrected-to-normal vision. For a subset of eight patients, the number of CAG-triplets was known. All patients received medication including antihyperkinetics/neuroleptics, either alone or in combination with antidepressants ($n = 5$), nootropics ($n = 5$), benzodiazepines ($n = 1$), and anti-Parkinsonian agents ($n = 1$). Screening for dementia was performed using the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975). Only two patients showed very mild signs of dementia while the others performed in the normal range. Relevant biographical and clinical data for each patient are listed in Table 1.

Since we have already documented HD patients' impairments in visual processing speed and WM storage capacity compared to age- and education-matched control subjects (Finke et al., 2006), we examined a control group only for the simultanagnosia task in the present study. The control group consisted of 10 healthy subjects (six male, four female). The relevant biographical data of the control group is again listed in Table 1. Neither age [$T(18) = 0.60$, $P > 0.55$], gender distribution [$\chi^2(1) = 0.22$, $P > 0.60$], years of education [$T(18) = 1.41$, $P > 0.15$], or MMSE values [$T(18) = 0.0$, $P > 0.95$] differed significantly from

the HD group. None of the control subjects reported any history of neurological or psychiatric disorders, and all had normal or corrected-to-normal vision.

2.2. Apparatus

In both the simultaneous-perception and the whole-report task, stimuli were presented on a personal computer with a 17 in. monitor (1024 × 768-pixel screen resolution; 70-Hz refresh rate). The viewing distance was approximately 50 cm. A well-padded chinrest was used to keep the head posture and viewing distance constant.

2.3. Simultaneous-perception task: stimuli, task, and procedure

In the simultaneous-perception task, the stimuli consisted of simple black line-drawing figures: a triangle, a square, a pentagon, a hexagon, a heart, a crescent, a cross, a star, and a circle. The stimuli were presented in black on a white monitor background. The displays used in the four different presentation conditions of the task (figures presented either alone, adjacent to each other, embedded within each other, or overlapping) are presented in Fig. 1.

The task consisted of four presentation conditions. (i) The single-item condition was introduced as a control condition to ascertain that a subject was generally able to correctly name all the line-drawing objects presented in the task, for each object size used. To test for this, the figures were presented in the largest and smallest sizes, as used in the multi-stimuli conditions (see below).

The multi-stimuli conditions (conditions 2, 3, and 4 below) consisted of 16 trials each, presenting displays with either two, three, four, or five figures simultaneously (four trials for each number-of-simultaneous-objects condition). (ii) In the adjacent-stimuli condition, the figures were presented side by side without overlap (see Fig. 1, A). (iii) In the embedded-stimuli condition, the

Table 1
Patient and control subject details

	Sex	Age	Hand	Education (years)	MMSE	Duration (years)	Onset (years)	Medication (CPZ)	Accessory diagnoses	CAG
Patient										
NH	M	37	R	9	25	3.5	34	400	F06.32	47
AS	M	42	R	10	30	10	32	600	F07.8; F02.2	50
PH	M	58	R	9	24	6	52	435	F06.32; F07.9	43
BH	F	51	R	10	29	4	47	375	F06.2	44
BS	M	38	R	9	30	10	28	180	F06.32	–
GW	M	44	A	10	30	2	42	180	F06.32	45
DH	F	49	R	9	29	4	45	300	F06.32	46
SJ	F	35	R	10	28	2	33	120	–	46
AB	M	30	R	10	29	1.5	29	200	–	48
JJ	M	35	R	9	30	3	32	300	–	–
Mean		41.9 (8.6)		9.5 (0.5)	28.4 (2.2)	4.6 (3.1)	37.4 (8.4)	309 (147)		46.1 (2.2)
Control subject										
MK	M	32	R	10	29	–	–	–	–	n. a.
RB	M	58	R	10	28	–	–	–	–	n. a.
KT	F	56	R	10	28	–	–	–	–	n. a.
EK	M	55	R	10	27	–	–	–	–	n. a.
HW	M	44	R	10	28	–	–	–	–	n. a.
ES	F	55	R	10	28	–	–	–	–	n. a.
SS	M	35	R	10	30	–	–	–	–	n. a.
UD	F	48	L	10	27	–	–	–	–	n. a.
RV	M	35	R	9	29	–	–	–	–	n. a.
KG	F	28	R	9	30	–	–	–	–	n. a.
Mean		44.6 (11.3)		9.8 (0.4)	28.4 (1.1)					

Hand: handedness according to the Edinburgh Handedness Inventory (Oldfield, 1971); education in number of years; MMSE: Mini Mental State examination total score; duration: duration of HD since first symptoms (in years); onset: age at onset of the clinical state of the illness (in years); medication (CPZ): neuroleptic potency of medication converted to chlorpromazine equivalents in mg/day; CAG: CAG-triplet repeat length on gene IT15 on chromosome 4p; F: female; M: male; R: right; A: ambidextrous L: left; F02.2: dementia in Huntington's disease; F06.2: organic delusional disorder; F06.32: organic depressive disorder; F07.8: organic personality and behavioural disorder; F07.9: unspecified mental disorder due to brain disease; n. a.: not assessed.

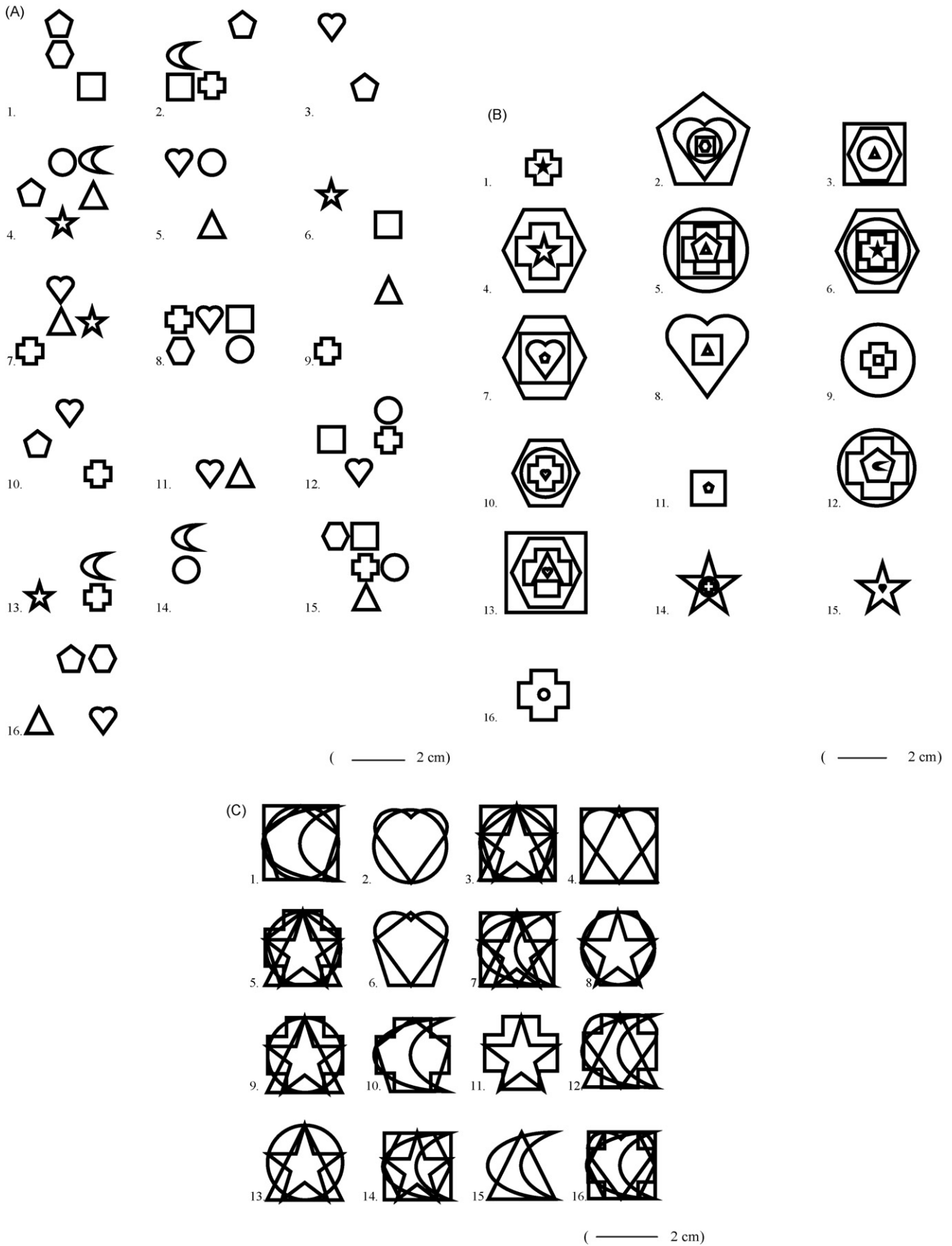


Fig. 1. Stimuli in the various conditions of the simultanagnosia test. (A) adjacent stimuli, (B) embedded stimuli, (C) overlapping stimuli.

smallest figure was enclosed by the lines of the next larger one and so forth, with the largest figure forming the outer boundary (see Fig. 1, B). (iv) In the overlapping-stimuli condition, the figures were comparable in size and presented one above the other (see Fig. 1C).

Each trial started with a red fixation point presented for 2 s in the center of the screen. Then, the fixation point was removed and the line-drawing objects were presented. In each presentation condition, the subject's task was to name each object present in the display without any time constraints. A trial was counted as 'correct' only if the subject reported each of the figures presented; if the subject left out or reported one or more of the figures incorrectly, the trial was counted as 'erroneous'. In addition, on each error trial, the exact number of missed or confused stimuli was recorded and the specific kinds of figures that were missed or confused were documented. After the subject had indicated that his/her answer was complete, the experimenter started the next trial.

2.4. Whole-report task: stimuli, task, and procedure

In the whole-report task, subjects were instructed to fixate a central white digit (0.3° of visual angle) presented for 300 ms on a black monitor background. Then, after a gap of 100 ms, red and/or green letters (0.5° high × 0.4° wide) were presented for a brief, pre-determined exposure duration. The letters were arranged in a single column of five equidistant stimuli, presented either 2.5° to the left or 2.5° to the right of fixation (see Fig. 2). The stimuli on a given trial were chosen randomly from the set {A B E F H J K L M N P R S T W X Y Z}, with a particular letter appearing only once. All subjects were shown the same letter displays in the same (random) order. Stimuli were presented either unmasked or masked. In unmasked conditions, the effective exposure durations are prolonged by several hundred milliseconds due to 'iconic' memory buffering (Sperling, 1960). In masked conditions, the letter array was superseded by masking stimuli, each one a square (of side length 0.5°) filled with a "+" and an "x", which were presented for 500 ms at each letter location. The post-array masks were shown to terminate the iconic letter representation.

Subject's task was to verbally report as many letters as possible. The letters could be named in any, arbitrary order, and there was no emphasis on report speed. Subjects were instructed to name only those letters they had recognized

'with certainty'. The experimenter entered the reported letters on the keyboard (in the reported order) and then initiated the next trial.

The whole-report experiment comprised two phases: in phase 1, three exposure durations were determined individually for each subject; in the experimental phase 2, the stimuli were presented to the subjects for these exposure durations and the data were collected. In more detail, in phase 1 (consisting of 24 trials), the exposure duration at which a particular subject could report on average one letter correctly was determined. This value was then used in phase 2 as the 'intermediate' exposure duration, along with a shorter (half as long) and a longer (twice as long) exposure duration. Then, in phase 2 (consisting of 192 trials), letter displays were presented for the three exposure durations, in either masked or unmasked conditions. The resulting six 'effective' exposure durations were introduced to sample response accuracy across a broad performance spectrum including the early as well as the late section of the subject's whole-report function. The exposure durations chosen were 300, 600, and 1200 ms for all HD patients except for BS (for whom 157, 300 and 600 ms were used). These rather long exposure durations reflect the inability to report letters at shorter exposure durations and therefore already indicate a severe slowing of perceptual processing speed.

Overall, there were 12 different trial conditions (2 hemi-fields × 3 exposure durations × 2 masking conditions), with 16 trials for each of the 12 conditions, presented in randomised order. From the whole-report functions, the TVA parameters for visual WM storage capacity and processing speed were then derived individually for each subject (see Kyllingsbæk, 2006).

3. Results

3.1. Simultaneous perception task

None of the subjects in either group made any errors in the single-item condition. For the various multi-stimuli conditions, the mean error percentages are presented in Fig. 3 as a function of the number of stimuli in the display (2, 3, 4, 5), separately for the HD patients and the control subjects. As can be seen, HD patients made errors under each presentation condition, whereas control subjects only showed errors when stimuli were presented in an overlapping fashion. Furthermore, in the overlapping-stimuli condition, the HD patients exhibited the most pronounced error rates which increased markedly with increasing number of stimuli.

That the overlapping-stimuli condition was particularly difficult for the HD patients is also evident from the single-case data listed in Table 2: 5 of the 10 HD patients made errors in the adjacent-stimuli condition, 5 in the embedded-stimuli condition, and all 10 in the overlapping-stimuli condition. Two patients (BS

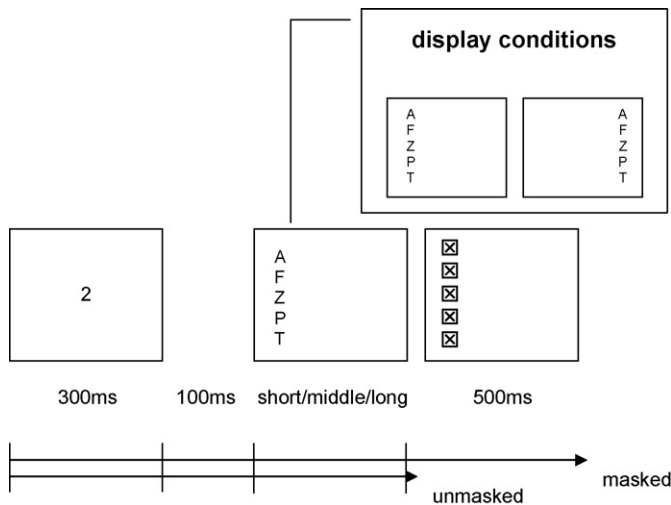


Fig. 2. Schematic representation of the whole report procedure and the possible display conditions. First, a digit is presented that has to be fixated by the subject. After a short ISI, the letter display is briefly presented with one of three different exposure durations (e.g. 86, 157, or 300 ms), either in the left or the right visual hemi-field (randomly determined). In masked trials, square masks are presented immediately at each previous letter position, constraining letter processing to their presentation time. In unmasked trials, due to visual persistence, letter processing is prolonged beyond their presentation time, by several hundred milliseconds. In this way, by using three exposure durations in either masked or unmasked trials, six effective exposure durations result. The subject's task is to report as many letters as possible.

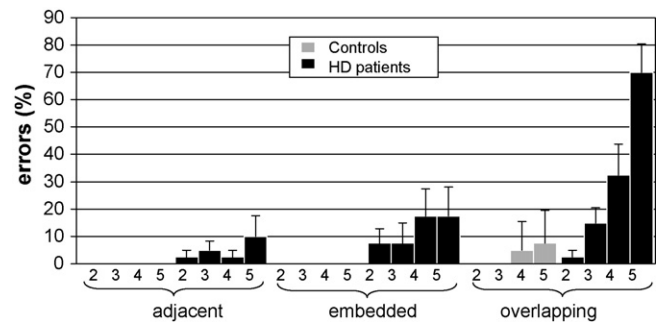


Fig. 3. Percentage of errors in the three multi-stimuli conditions of the simultaneous test (adjacent stimuli, embedded stimuli, and overlapping stimuli) for the different stimulus numbers (2, 3, 4, 5), separately for the Huntington's disease patient and the control group. Error bars indicate the standard errors.

Table 2
Percentage of errors in the different conditions of the simultanagnosia test

	Single stimuli	Adjacent stimuli	Embedded stimuli	Overlapping stimuli
Patients				
NH	0	25.00	18.75	43.75
AS	0	0	6.25	43.75
PH	0	0	0	37.50
BH	0	0	6.25	18.75
BS	0	6.25	0	6.25
GW	0	12.50	18.75	6.25
DH	0	6.25	0	31.25
SJ	0	0	0	43.75
AB	0	0	0	6.25
JJ	0	31.25	75.00	68.75
Mean (S.D.)	0(0)	8.13 (11.43)	12.50 (23.20)	30.63 (20.93)
Controls				
MK	0	0	0	0
RB	0	0	0	0
KT	0	0	0	0
EK	0	0	0	0
HW	0	0	0	0
ES	0	0	0	0
SS	0	0	0	12.5
UD	0	0	0	6.25
RV	0	0	0	12.5
KG	0	0	0	0
Mean (S.D.)	0(0)	0(0)	0(0)	3.12 (5.31)

and AB) performed within the range of the (normal) control subjects in each of the multi-stimuli conditions.

To compare the performance between the patient and control groups in the various multi-stimuli conditions, a mixed-design ANOVA was carried out with the within-subject factors stimulus condition (adjacent, embedded, overlapping) and stimulus number (2, 3, 4, 5) and the between-subject factor group (HD patients, control subjects). This ANOVA revealed all main effects and two-way interactions to be highly significant (all P s < 0.01; lowest F -value = 7.23). The three-way interaction stimulus condition \times stimulus number \times group was also highly significant [$F(6,13) = 15.59, P < 0.01$].

The three-way interaction was analysed further by conducting separate ANOVAs for the three different stimulus conditions, each with the within-subject factor stimulus number and the between-subject factor group.

The ANOVA for the adjacent-stimuli condition failed to reveal any significant effects: stimulus number, $F(3,16) = 0.84, P > 0.45$; group, $F(1,18) = 2.67, P > 0.10$; stimulus number \times group, $F(3,16) = 0.84, P > 0.45$.

Similarly, there were no significant effects for the embedded-stimuli condition: stimulus number, $F(3,16) = 2.67, P > 0.10$; group, $F(1,18) = 2.90, P > 0.10$; stimulus number \times group, $F(3,16) = 2.67, P > 0.10$.

In contrast, for the overlapping-stimuli condition, all effects turned out to be highly significant: stimulus number, $F(3,21) = 25.10, P < 0.01$; group, $F(1,23) = 26.31, P < 0.01$; stimulus number \times group, $F(3,21) = 15.46, P < 0.01$. Post hoc comparisons revealed the HD patients to perform highly significantly worse, compared to the control subjects, in the condition

with five simultaneous stimuli [$T(18) = 5.64, P < 0.01$]; they performed significantly worse with 4 and 3 stimuli [4 stimuli: $T(18) = 2.35, P < 0.05$; 3 stimuli: $T(18) = 2.71, P < 0.05$]; but not with 2 stimuli [$T(18) = 1.00, P > 0.30$]. In addition, the HD patients exhibited a highly significant increase in errors with increasing stimulus number [$F(3,7) = 22.45; P < 0.01$], whereas the control subjects did not [$F(2,8) = 1.71; P > 0.20$]. While the HD patients exhibited a significant or marginally significant increase in errors when the number of stimuli was increased from 2 to 3 [$T(9) = 3.00, P < 0.05$] and 3 to 4 [$T(9) = 2.09; P < 0.10$], respectively, they showed a highly significant increase when the stimulus number was increased from 4 to 5 [$T(9) = 4.03, P < 0.01$] (Bonferroni-corrected post hoc comparisons).

To examine the errors made by the HD patients in more detail, error trials were characterized more specifically as either (a) omission errors: missing one or more presented stimuli, or (b) 'confusion' errors: replacing a presented stimulus by another, non-presented, one from the stimulus set (e.g., mistaking a presented cross for a non-presented square). The omission rates were 0%, 5.00% (S.D. = 9.22), and 21.25% (S.D. = 14.19) of all trials in the adjacent-, embedded-, and overlapping-stimuli conditions, respectively, and the confusion rates 8.13% (S.D. = 11.43), 7.50% (S.D. = 16.08), and 9.38% (S.D. = 9.02), respectively.

3.2. Whole-report test

For each subject, the raw data in the whole report experiment, that is the number of letters reported correctly at the different array exposure durations, was quantitatively described by TVA

Table 3

TVA whole-report parameters for HD patients: estimates of processing speed *C* and WM storage capacity *K*

	C	K
Patients		
NH	5.69	3.93
AS	3.98	2.75
PH	3.62	2.70
BH	8.32	3.85
BS	16.89	2.98
GW	6.45	4.00
DH	5.60	1.00
SJ	8.07	4.00
AB	16.00	3.95
JJ	6.00	2.84
Mean (S.D.)	8.06 (4.67)	3.20 (0.96)

Note. *C*: processing speed (elements/s); *K*: visual working memory capacity (number of elements).

model fitting, which produced individual estimates for processing speed *C* and WM storage capacity *K*. The probability of identification is modeled by an exponential growth function, in which the growth parameter reflects the rate at which the stimuli (objects) can be processed (processing speed *C*: number of elements/s), and the asymptote of the growth function indicates the maximum number of objects that can be represented within WM (WM storage capacity *K*).

Table 2 lists the parameters for TVA's best fits, based on a maximum-likelihood procedure, to the data of each HD patient. Processing speed for the left (C_L) and for the right (C_R) visual hemi-field were originally estimated separately as the summed *v* values for the objects presented to the left and to the right of fixation, respectively. However, since rather long exposure durations were used for each patient (see above) a hemi-field-specific analysis was deemed inappropriate and we computed the average value reflecting the general processing speed *C*, i.e. the total rate of information uptake (number of objects per second) across both hemi-fields. Analogously, we also computed the general WM storage capacity *K* across the two hemi-fields.

Table 3 lists the whole-report TVA parameter estimates for each HD patient. The present HD patients' visuo-perceptual processing speed averaged 8.1 letters/s. That is, they required approximately 125 ms to perceive a single letter, which is very similar to those of a larger group of patients and far below the performance of normal subjects of a comparable age (~25 elements/s; see Finke et al., 2006, for comparison of HD patients' and controls' values). Furthermore, the patients' visual WM storage capacity averaged 3.2 elements. This value is also (somewhat) reduced compared to normal subjects, who are able to maintain nearly four elements in visual WM (Cowan, 2001; Finke et al., 2006).

Interestingly, as can be seen from Table 3, the two patients who showed no or only single errors in each sub-condition of the simultanagnosia task, BS and AB, were also those who exhibited the fastest processing speed (i.e., the greatest number of objects processed per second). Their rate of information uptake per second was at least twice as high as that of all other patients.

Table 4

Correlations between the TVA whole-report parameter estimates for visuo-perceptual processing speed and visual working memory capacity and the various multi-stimuli conditions of the simultanagnosia task in HD patients

	Adjacent stimuli	Embedded stimuli	Overlapping stimuli
<i>C</i>	-0.22	-0.26	-0.65*
<i>K</i>	0.02	0.02	-0.25

Note. *C*: processing speed (elements/s); *K*: visual working memory capacity (number of elements). * $P < 0.05$ (1-sided).

3.3. Correlations of simultaneous perception with whole-report performance and with the clinical and demographic data of the HD patients

Table 4 lists the correlations between HD patients' TVA parameter estimates for visual processing speed and, respectively, WM storage capacity on the one hand and errors in the various multi-stimuli conditions of the simultaneous perception task on the other. The only significant, negative correlation was that between processing speed *C* and the percentage of errors in the overlapping-stimuli condition of the simultanagnosia task: the lower the processing speed the more errors occurred in identifying multiple overlapping-figures. All other correlations were non-significant (all $P > 0.45$).

No significant correlations were found between the errors in any of the multi-stimuli conditions of the simultaneous perception test and demographic variables such as age, MMSE value, duration of the clinical phase of the illness, medication dosage (converted to chlorpromazine equivalents according to Rijcken, Monster, Brouwers, de, & van den Berg, 2003), age at onset, or CAG repeat length (all $P > 0.20$). The five patients with an accompanying depressive disorder (see Table 1) did not make significantly more errors in any condition compared to the other patients (all $P > 0.40$).

4. Discussion

4.1. Simultanagnosia in Huntington's disease

One aim of the present study was to examine whether HD patients with severe reductions in visuo-perceptual processing speed and visual WM storage capacity, comparable in magnitude to patients with simultanagnosia (Duncan et al., 2003), would show impaired simultaneous perception. Simultanagnosia has been documented repeatedly in patients with various forms of 'cortical' dementia such as Alzheimer's disease and, especially, posterior cortical atrophy (Huberle & Karnath, 2006; Rizzo & Vecera, 2002; Tang-Wai et al., 2004). However, thus far, to our knowledge, there have been no reports of HD patients suffering from a similar impairment in identifying multiple objects presented simultaneously.

In the literature, a number of similarities between HD and simultanagnosia patients have been noted with respect to oculomotor, visuo-motor, and visuo-spatial behavior. These include difficulties in initiating saccades, gaze fixation abnormalities with intrusions of small jerky saccadic displacements, and

abnormal undershooting of saccade targets (Harper, 1991), as well as deficits in spatial perception (dot counting and location judgments; Ho et al., 2003a) and problems with reading, writing, and visuo-construction (Brandt, 1991). Strikingly, HD patients (Roman et al., 1998), like patients with Bálint's syndrome (Huberle & Karnath, 2006; Pavese et al., 2002; Rafal, 1997), are severely impaired in identifying Navon-type hierarchical stimuli in which the global shape of a figure is inconsistent with its local elements (e.g., the letter A made out of small H's), compared to when it is consistent.

The present study revealed HD patients to be indeed impaired in a test of simultaneous perception of multiple objects, even under free viewing conditions without any time constraints (i.e., with unrestricted viewing time). All HD patients examined were able to identify the figures when presented singly in the smallest as well as the largest sizes used under multi-stimulus conditions. That is, they did not suffer from visual acuity deficits or object agnosia preventing the recognition of individual objects. Also, they were generally able to report multiple stimuli that were either presented adjacent to each other or in an embedded manner, although their report was slow and they tended to perform worse than the control subjects in the latter condition. However, the HD patients showed a pronounced deficit compared to the control subjects of comparable age in reporting multiple stimuli when these were presented in an overlapping manner. This deficit cannot be attributed to generalized intellectual deterioration, as the patients' MMSE scores were comparable, on average, to those of the control group and indicated no or only very mild signs of dementia. These values obtained in our patients reflect those of Lemiere, Decruyenaere, Evers-Kiebooms, Vandenbussche, and Dom (2004) who did not find intelligence deterioration during the course of HD. Furthermore, it is important to note that the MMSE values in our group and the duration of the disease's clinical phase were not correlated with the error rates, indicating that is not a general cognitive decline which causes deficits of simultaneous perception. Likewise, the impairment cannot be attributed to medication, as the patients' medication dosages were also uncorrelated with their error rates.

On 'error' trials, HD patients normally omitted just one or two items (except for three 'extreme' three-item misses in the overlapping-figure condition). On this criterion, most of our patients would not be classified as suffering from severe deficits of simultaneous perception, comparable, for example, to the classical cases described by Balint (1909), but rather from a 'mild' form only (Hécean & De Ajuriaguerra, 1954). Note, though, that the present test used free viewing conditions without any time restrictions, in contrast with most other studies of simultanagnosia patients, in which stimulus exposure duration was limited (e.g., Coslett & Saffran, 1991; Huberle & Karnath, 2006; Pavese et al., 2002). Therefore, it is likely that a speeded version of the test would have revealed more severe deficits for the present HD patient group. Also, it is plausible to assume that, under time-restricted viewing conditions, the patients' ability to report adjacent and, especially, embedded stimuli would have been impaired as well as their report of overlapping stimuli.

The results suggest that HD patients, like patients suffering from simultanagnosia, may perceive complex visual scenes containing many simultaneously present objects in a piecemeal fashion (with an erratic focus on only one or very few items) such that the scene is processed as a series of single unrelated objects (Rizzo & Vecera, 2002). One implication of the present findings is that tasks using complex visual stimulus material may be inappropriate for the assessment of cognitive functions in symptomatic HD patients. Thus, for example, in a number of 'executive' tasks used to assess deficits of higher cognitive abilities, impaired performance exhibited by HD patients may result from more basic deficits in processing multiple stimuli in parallel (e.g., Lawrence et al., 1996).

4.2. Attentional deficits underlying simultanagnosia

The results of the present study also suggest that cases of simultanagnosia may be more frequent than assumed hitherto (e.g., Coslett & Saffran, 1991). Indeed, Rizzo and Vecera (2002) have already stated that simultanagnosia might most commonly result from neurodegenerative diseases, and they advocated for a new, group study-based approach (instead of the most frequently used single-case approach) for research on this disorder and its underlying attentional deficits. This approach was followed in the present study, where group analyses permitted us to systematically correlate the performance deficits in the simultaneous perception test with the severity of reductions in attentional functions assumed to underlie these deficits.

The majority of the HD patients examined in the present study showed the characteristic deficits of simultaneous perception. However, there was a substantial variability in performance: while three patients showed no or only single errors in all conditions, one patient (JJ) showed severe impairments in the embedded- as well as the overlapping-figure condition. This inhomogeneity with respect to simultanagnosia symptoms enhanced the probability of finding significant correlations with 'critical' attentional functions measured by the (independent) TVA parameters processing speed and WM storage capacity, both estimated based on patients' performance in a whole-report task with brief presentation of a letter array.

The percentage of errors made in the overlapping-figure condition was inversely related to the TVA parameter visuo-perceptual processing speed. This suggests that the marked slowing of perceptual processing in HD patients gives rise to impaired perception of multiple (in particular, overlapping) stimuli. In contrast, the (slightly) reduced visual WM storage capacity was not found to be related to the impaired report of multiple (overlapping) figures, suggesting that WM storage capacity did not contribute significantly to the deficit in multi-stimulus identification. This pattern is consistent with Duncan et al. (2003) who found the clinical symptoms of simultanagnosia to be primarily related to reductions in processing speed, and with Huberle and Karnath (2006) who found that a reduction of WM storage capacity cannot, at least, be the sole cause of simultanagnosia. Consequently, the present findings do not support the view of Coslett and Saffran (1991) that a failure to report simultaneous objects is caused by a failure to establish

integrated representations of multiple objects in a visual WM store.

The substantial (negative) correlation between HD patients' performance in recognizing overlapping stimuli and their reduced visuo-perceptual processing speed suggests that speed of processing may be indeed a critical variable underlying the manifestation of simultanagnosia symptoms. In biased-competition models of visual attention such as TVA, objects present in multi-stimulus displays resembling everyday scenes are assumed to compete for being encoded into visual WM (Desimone & Duncan, 1995). According to TVA (Bundesen, 1990), a limited amount of processing capacity is distributed amongst competing objects and only those objects that are processed fastest gain access to visual WM. In case of severe reductions of the available processing capacity, perceptual failure seems to occur then for all but the most salient objects (Duncan et al., 2003).

4.3. Visuo-perceptual slowing and recognition of overlapping-figures

For the present group of HD patients (and also for the individual patients, except for JJ), there was no or only minor evidence of impaired simultaneous perception when stimuli were presented adjacent to or embedded within each other. This result pattern is strikingly similar to that reported by Humphreys and Price (1994) in two cases of simultanagnosia: their patients were quite unimpaired in reporting two figures when these were presented in an adjacent manner and with unlimited viewing time. However, when presentation duration was reduced, performance decreased. Importantly, when two figures were presented in an overlapping manner, performance was also reduced, even with unlimited presentation times. Humphreys and Price (1994) concluded that their patients suffered from an impairment in the perceptual grouping of visual features and in figure-ground segmentation. Consistent with this, a number of other studies have also shown that patients with simultanagnosia have problems especially in identifying overlapping-figures (Riddoch & Humphreys, 2004; Valenza et al., 2004). Furthermore, simultanagnosia patients may also fail to identify single objects composed of multiple parts (Humphreys & Price, 1994) and single objects that are segmented into parts by some additional lines (Riddoch & Humphreys, 2004).

This pattern of effects raises a general question: how can a deficit in perceptual processing speed selectively affect the report of overlapping-figures (despite unlimited viewing time), while relatively sparing the (albeit slow) report of multiple figures presented in an adjacent or an embedded fashion? When visuo-perceptual processing is slow, as in the majority of the present patients, a good adaptation might be to reduce competition among multiple objects by using serial top-down controlled selection of one display location after the other (see Duncan et al., 2003, for a similar argument as to how letter-by-letter reading in ventral simultanagnosia might arise from slowing of visuo-perceptual processing). Restricting limited processing resources to one location increases the probability of successful visual short memory entrance and report. Consistent with this,

patients with simultanagnosia have been reported to perceive the world in a piecemeal fashion (Paterson & Zangwill, 1944), with the focus of processing being restricted to only one stimulus at a time (Rizzo & Vecera, 2002). Such a strategy might be particularly suitable for displays with multiple objects presented adjacent to each other, under conditions of unlimited viewing time. And it might also be suitable to conditions with embedded figures, where a strategy to start with either the outermost or the innermost (embedded) object and to then report, one after the other, the next smaller or, respectively, larger object could substantially improve performance. Indeed, all patients exhibited a sequential report progression of this type.

But can slowing of visuo-perceptual processing also account for the HD patients' marked performance deficit in the overlapping-figure condition, especially the systematic increase in (omission) errors with increasing stimulus number? Serial, top-down controlled selection of one display location after the other might be inappropriate with complex backgrounds and with objects segmented into parts by overlapping contours of other objects. If limited processing resources are restricted to one location in order to maximize the speed of processing at this location then two overlapping objects will have to share processing capacity. Consequently, each object gets less capacity and has a lower chance to reach visual short-term memory. Identifying one or two elements in such a demanding display may exhaust the patients' limited perceptual processing capacity (see Humphreys & Price, 1994; Riddoch & Humphreys, 2004). Thus, if the patients attempt to divide their perceptual capacity among a larger number of objects, they would make errors—because the capacity available for each object would be insufficient for the depth of discrimination required for object identification. As a result, only the most dominant objects may survive the competition for awareness, while the other objects are 'lost'. Consistent with this view, the number of omission errors was particularly increased in the overlapping-stimuli condition (21.25%).

4.4. Neuro-anatomical pathology underlying simultanagnosia in Huntington's disease

Cognitive decline in HD has been related to the dopaminergic system. In particular, increasing loss of D2 receptor densities in the striatum has been shown to be strongly associated with impaired performance in a number of cognitive tasks assessing, among other functions, processing speed and working memory (Bäckman & Farde, 2001). In accordance with such findings, in our previous study of HD patients (Finke et al., 2006), we found a significant relationship between disease duration and the decrease in TVA based measures of perceptual speed and working memory storage capacity. Therefore, it is tempting to speculate that the present finding of impaired simultaneous perception of overlapping shapes also reflects declining dopaminergic neurotransmission within cortico-striatal circuits. On the other hand, in our current study only processing speed, but not working memory storage, was significantly associated with the ability of simultaneously perceiving visual objects. Other studies applying a different paradigm (the inspection time task)

to assess perceptual processing speed have demonstrated a close link to the cholinergic system (Hutchison, Nathan, Mrazek, & Stough, 2001; Nathan & Stough, 2001) but no evidence in favour of a significant involvement of dopamine (Johnson et al., 2004). This raises the possibility that HD subjects' impaired performance might be more related to cholinergic neurotransmission. In fact, the cholinergic system is assumed to have a decisive role in the attentional processing of sensory stimuli. It has been suggested that cortical cholinergic inputs mediate early steps in information processing by amplifying the neuronal response to sensory stimulation (Sarter & Bruno, 1999). Animal studies have clearly demonstrated that such a gain in stimulus processing is related to a cholinergically mediated retuning of receptive fields and the resulting expansion of cortical stimulus representation (Sarter, Hasselmo, Bruno, & Givens, 2005). Such data nicely fit the ideas of Bundesen et al. (2005) in their neural interpretation of TVA ('NTVA'). According to NTVA, processing capacity is directly related to the number and the activation of cortical neurons devoted to the processing of a visual object. A gain in processing speed thus would reflect an increase in the cortical capacity for representing objects which is modelled by NTVA as an attentional-weight related adaptation of receptive fields. The cortical cholinergic excitation originating from the basal forebrain nucleus is controlled by a double-step inhibitory pathway that starts with a dopaminergic nigrostriatal input (Sarter & Bruno, 1999). Due to the loss of presynaptic dopaminergic input to the basal ganglia in HD, down regulation of cortical cholinergic excitation could be the net effect within this circuitry, giving rise to a severe diminution of the number of objects that can be simultaneously represented within the visual processing system. This inability would be reflected in the strong reduction of processing speed we found in the present study. Of course, this cholinergic interpretation, which in effect is just an extension of the dopaminergic interpretation of cognitive decline, is rather speculative at the moment and clearly requires more research. For example, it would be interesting to see whether a similar result as that obtained in HD patients in the present study, can be observed in patients suffering from Alzheimer's disease, where damage to the cholinergic projection system is a major hypothesis explaining the development of dementia.

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