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Behavioural Neurology

Graph methods to infer spatial disturbances: Application to Huntington's Disease's speech



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ABSTRACT

Objective: Huntington's Disease (HD) is an inherited neurodegenerative disease caused by the mutation of the Htt gene, impacting all aspects of living and functioning. Among cognitive disabilities, spatial capacities are impaired, but their monitoring remains scarce as limited by lengthy experts' assessments. Language offers an alternative medium to evaluate patients' performance in HD. Yet, its capacities to assess HD's spatial abilities are unknown. Here, we aimed to bring proof-of-concept that HD's spatial deficits can be assessed through speech.

Methods: We developed the Spatial Description Model to graphically represent spatial relations described during the Cookie Theft Picture (CTP) task. We increased the sensitivity of our model by using only sentences with spatial terms, unlike previous studies in Alzheimer's disease. 78 carriers of the mutant Htt, including 56 manifest and 22 premanifest individuals, as well as 25 healthy controls were included from the BIOHD & (NCT01412125) & Repair-HD (NCT03119246) cohorts. The convergence and divergence of the model were validated using the SelfCog battery.

Results: Our Spatial Description Model was the only one among the four assessed approaches, revealing that individuals with manifest HD expressed fewer spatial relations and engaged in less spatial exploration compared to healthy controls. Their graphs correlated with both visuospatial and language SelfCog performances, but not with motor, executive nor memory functions.

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Conclusions: We provide the proof-of-concept using our Spatial Description Model that language can grasp HD patient's spatial disturbances. By adding spatial capabilities to the panel of functions tested by the language, it paves the way for eventual remote clinical application.

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1. Introduction

Huntington's Disease (HD) is an autosomal dominant neurodegenerative disorder caused by a repeated expansion of the CAG trinucleotide (≥ 39 repeats) in the Huntingtin gene (Tabrizi et al., 2019). It is characterized by motor, cognitive, and psychiatric symptoms. The evolution of HD includes an asymptomatic pre-manifest phase (preHD) and a manifest phase with symptoms gradually affecting patients' daily living, before leading to death within 35 years after clinical onset (Walker, 2007).

Among daily impairments in HD, individuals have reported spatial abilities deficits, which refers to the way individuals mentally represent and manipulate spatial information (Shah & Miyake, 2005). These deficits include visuo-perceptual, visuo-constructive, visual scanning, and mental rotation difficulties, starting before clinical onset. This causes confusion in daily functioning, which can influence overall cognitive performances (Coppen et al., 2018). Although spatial disorders are less common in HD compared to diseases like Alzheimer's, it is likely undervalued, especially since significant occipital atrophy is evident even in the preHD stage of the disease (Scahill et al., 2013). However, due to the challenges associated with monitoring spatial capacities, this atrophy and its consequences have not been thoroughly explored.

Spatial deficits are traditionally measured with pen-and-pencil tests during neuropsychological assessments (Brandt et al., 2004; Gómez-Tortosa et al., 1996; Lawrence et al., 2000). However, individuals with HD often face limited access to appropriate healthcare systems and lengthy comprehensive assessments involving a multidisciplinary clinical team. This can lead to poor symptom management and a reduction of individuals' quality of life (Frich et al., 2016; van Lonkhuizen et al., 2023). Because it is easily collectible, brief, and examiner-free, speech is thought as the best candidate to assess patients' performances remotely and will see greater utilization in future healthcare systems (Fagherazzi et al., 2021; Robin et al., 2020). In HD, it has been shown that speech can predict patients' disease progression, motor, and functional performances, as well as cognitive functions such as attention, executive functions, and cognitive flexibility (Riad et al., 2020, 2022; Romana et al., 2020; Vogel et al., 2012). However, to make it a more complete tool and optimize its future use, it remains to assess its ability to test HD patients' visuospatial performance.

Several studies have yet demonstrated that spatial language is a specific domain within language. Spatial language translates spatial representation in language by using spatial terms, i.e., spatial prepositions and action verbs, to describe

the spatial relations between objects (Chatterjee, 2008; Landau & Jackendoff, 1993). Descriptions of objects' spatial relations are influenced by the referential position of the object in space, with entities positioned on the left being more frequently mentioned first than those on the right in a scene in healthy individuals (Baltaretu et al., 2016). Processing spatial language involves brain activity in the occipito-parietal stream which supports the “where pathway”, whereas object semantics activates the occipito-temporal stream which supports the “what pathway” in neuroimaging studies (Conder et al., 2017; Rocca et al., 2020). The ability to use appropriate language to describe a visual scene correlates with the acquisition of spatial abilities in children (Bowerman et al., 1995; Miller et al., 2017), as well as its decline with normal aging showing that language grasps visuo-spatial capacities (Ardila & Rosselli, 1996; Markostamou & Coventry, 2022). Likewise, cerebral lesions may yield difficulties in production and understanding spatial terms (Tranel & Kemmerer, 2004). Lastly, language allows the encoding of spatial representation, as demonstrated by the ability to create geographical maps from written corpora (Friedman et al., 2002; Louwerse & Zwaan, 2009). Embodiment based on sensorimotor interaction could also offer a conceptual spatial shortcut in the hypothesis of symbolic interdependence (Louwerse, 2011). Altogether, these findings suggest that spatial language reflects individuals' spatial abilities.

This has triggered the use of the Cookie Theft Picture (CTP) description task to assess spatial abilities through, in which participants are required to scan, infer relationships between pictorial elements, and report them orally (Goodglass & Kaplan, 1972). Thus, three studies were run in Alzheimer's disease, each focusing on various aspects of spatial language (Fig. 1). First, the Spatial neglect method enabled classifying Alzheimer's individuals from controls by counting the number of times each pictorial elements are mentioned in the different divisions of the picture (Masrani, 2018). Attention, concentration, repetition, and perception scores were then calculated based on the occurrence of the mentioned pictorial elements without considering the spatial relations between the elements in the descriptions. Secondly, Bosse's study described the frequency of spatial prepositions that characterized location and direction of pictorial elements in Alzheimer's individuals CTP descriptions. The frequency was lower for left/right, directional, and dynamic prepositions compared to healthy individuals. However, action verbs were not assessed, excluding some spatial and directional information held by these action verbs (Bosse, 2019). Because both methods, partially integrated spatial context, Ambadi et al. proposed the Spatio-semantic model using graph theory for Alzheimer's CTP description analyses. Graph theory is a

		CTP descriptions characterised by	Spatial terms	Pictorial elements mentioned	Selectivity for spatial relations only
COMPARATIVE METHODS	Spatial terms frequency (Bosse, 2019)	Spatial prepositions	✓	✗	✗
	Spatial neglect (Masrani, 2018)	Attention Concentration Repetition Perception	✗	✓	✗
	Spatio-semantic graph model (Ambadi et al., 2021)	Visual narrative path	✗	✓	✗
DESIGNED METHOD	Spatial Description graph model	Spatial representation of the CTP based on spatial terms	✓	✓	✓

Fig. 1 – Comparison between methods capturing spatial information from spoken language production of the Cookie theft picture (CTP).

mathematical framework, which represents a network of nodes (the pictorial elements like objects, people, location etc.) connected by arrows according to the order of the description (called edges in graph theory). Whereas this model distinguishes Alzheimer's and healthy individuals by reflecting their descriptions' visual narrative paths, attentional, and organizational abilities (Ambadi et al., 2021), it does not assess spatial prepositions and action verbs. Therefore, in “The boy is wearing trousers and the mother a dress. This girl is on the left side of the boy, wearing a skirt”, the Spatio-semantic approach models the entire path between the mentioned elements encompassing the single spatial relation with the non-spatial descriptions (Boy → Mother → Girl → Boy), thus accounting for three semantic relations rather than a single spatial one. This might artificially increase the representation of each element as a spatial object despite the fact the utterance is not expressing a spatial relation and could constitute a caveat in perseverative patients.

Therefore, considering the low spatial disturbances and high perseverative behavior in HD compared to AD (Coppin et al., 2018; Rosenblatt et al., 2007), to ensure capturing the spatial deficit in HD strengthening the Spatio-semantic model appears necessary. Here, we thus developed the Spatial Description Model, a comprehensive language-based assessment of spatial disturbances, selectively considering only sentences that contain spatially relevant information before modeling them graphically. The Model operated by removing sentences without any information about the pictorial elements' location or their spatial relations. It maximized the extraction of spatial information by integrating together the mentioned pictorial elements with spatial language. Spatial relations were identified by detecting labeled spatial terms, pictorial elements, and determining if they were used together to describe the picture spatially. Thus, using the previous example, our algorithm would identify only a single spatial relation (Girl → Boy) rather than three. To validate our

Model, we assessed its convergence/divergence validity using the SelfCog battery in a cross-sectional cohort of HD carriers and control participants (Lunven et al., 2023). In addition, we checked the added value of our model by comparing its performance with the ones developed in Alzheimer's disease (Fig. 1).

2. Material & methods

2.1. Participants

We enrolled 81 HD gene carriers (CAG ≥ 38), including 19 preHD and 59 manifest HD at an early disease stage (stage I or II) (Shoulson, 1981), and 25 healthy controls (HC) without any cognitive deficits (Mattis Dementia Rating Scale score ≥ 136) (Mattis, 1976) from two observational cohorts (Repair-HD NCT03119246 & BIO-HD NCT01412125) at the Henri Mondor Hospital (Créteil, France). PreHD participants were defined by a Total Motor Score (TMS) ≤ 5 and a Total Functional Capacity (TFC) = 13 (Kremer & Huntington Study Group, 1996; Tabrizi et al., 2009). All participants were French native speakers, aged above 18 who had signed an informed consent. Exclusion criteria were incapacity to consent, and significant neurologic or psychiatric comorbidities unrelated to HD. Ethics approval was given by the institutional review board from Henri Mondor Hospital (Créteil, France) for the BioHD cohort and the CPP Saint Louis French part of the Repair-HD cohort, in compliance with the Helsinki Declaration.

2.2. Participants assessment

2.2.1. General assessment

All participants were evaluated with the Huntington's Disease Rating Scale © (UHDRS) which included the TMS, TFC, Functional Assessment Scale and a cognitive evaluation (Symbol

Digit Modalities Test (SDMT), Letter fluency (1 min), Stroop test (word, color and interference) (Butters et al., 1986; Huntington Study Group, 1996; Jensen, 1965; Smith, 1982; Strauss et al., 2006). The Categorical fluency test (over 1 min) was also added. Disease severity was defined using the composite UHDRS (cUHDRS) (equation (1)) and Disease Burden Score (DBS) (equation (2)) (Penney Jr et al., 1997; Schobel et al., 2017). The preHD group estimated onset to motor symptoms was predicted based on their CAG repeats (Langbehn et al., 2004). Group differences were assessed using ANOVAs and Tukey's post-hoc analysis.

$$cUHDRS = \left(\frac{TFC - 10.4}{1.9} - \frac{TMS - 29.7}{14.9} + \frac{SDMT - 28.4}{11.3} + \frac{Stroop\ word - 66.1}{20.1} \right) + 10 \quad (1)$$

$$DBS = age \times (CAG - 35.5) \quad (2)$$

For convergence and divergence validity between the Spatial Description Model's graph features and cognitive measures, 22 HD participants also performed the digitized cognitive SelfCog © battery that tested motor, executive, spatial, language and memory functions in 15 min (Lunven et al., 2023). The sample of participants were similar to the rest of the HD participants (Appendix 2. Supplementary Table 7). In this battery, all functions are measured according to the same paradigm. For each trial of each subtest, the input stimuli (two images presented on the screen) and output responses (pressing a key) are similar, the only variations being the instructions. It allowed to subtract the mean motor response time (RT) from the cognitive ones to avoid confounding motor impairment from cognitive processing. The Inverse Efficiency Score (IES) measure was used for each cognitive function consisting of the mean cognitive RT corrected by the motor RT divided by the test accuracy.

2.2.2. The Cookie Theft Picture description task (CTP)

French verbal descriptions of the CTP were recorded by a trained neuropsychologist using a microphone for subsequent transcription and analysis. Participants were shown the CTP picture and instructed "Please tell me everything you see happening in this picture". The recordings were stopped when the participants indicated they finished or according to a time limit of 5 min. The recordings were transcribed by speech therapists using Praat and Seeshat softwares (Boersma et al., 2001; Titeux et al., 2020). For subsequent analyses, language fillers, stuttering, unintelligible words, nonlinguistic additions, and pauses were excluded from transcripts.

2.3. The Spatial Description Model

The Spatial Description Model produced a graphical representation of a participant's CTP spatial description.

2.3.1. Spatial annotation

The CTP is composed of multiple pictorial elements that constitute the scene. The major pictorial elements are referred to as Information Unit (IU). Based on healthy subjects' picture description, the list of IUs was composed with

11 objects, 4 persons/groups and 2 locations (Appendix 1. Supplementary Table 2) (Croisile et al., 1996; Lindsay et al., 2021). The IUs in the transcript of CTP descriptions were manually labeled by one of the authors prior to any analysis using the defined IUs list (Appendix 1. Supplementary Table 2), which instructed how to handle the different naming possibility of an IU. For example, if the term used make direct reference to an IU (for example 'Women' for the IU "Mother"), it is a valid synonym, accounting for that IU. Similarly, spatial prepositions or action verbs were labeled as spatial terms (Appendix 1. Supplementary Table 3). The annotation inter-rater reliability of descriptions was carried out on 12 participants' descriptions by 3 independent raters. The agreement was assured with an average Cohen's Kappa score of .69, considered a substantial agreement following McHugh (2012).

2.3.2. Spatial selectivity

To achieve spatial selectivity and avoid the Spatial Description algorithm to integrate non-spatial elements, the Model integrated a preprocessing step on the labeled descriptions. Here, sentences that did not link two IU labels with a spatial term label were filtered out by the Model. This enabled the Model to extract only sentences that carried spatial information, hence, spatial descriptions. These were then used to generate the Spatial Description graphs.

2.3.3. Spatial description graphs

The spatial descriptions were transformed into graphs using Python's NetworkX package (Hagberg et al., 2008) (Fig. 2). Before processing an individual's spatial description, an initial graph was first generated where all possible IUs (e.g., "Boy", "Girl", "Cookie" etc. see Appendix Supplementary Table 2) are represented graphically by a node with an initial weight of 0. Each occurrence of spatial relations of that IU, adds a weight (+1) to the node, allowing to count the number of occurrences for each IU. In addition, each node is associated with a fixed pair of coordinates according to the IU's location on a CTP picture of 546 × 190 pixels. Each graph node was attributed a quadrant position (top-left in light blue, top-right in red, bottom-left in green, bottom-right in yellow, and virtual in grey). A virtual quadrant was created to account for IUs mentioned in sentences using spatial terms without explicit reference to a second IU. In the example "The water is falling down", falling down is an action verb and water an IU associated to the virtual quadrant as there is no second referential IU. This quadrant was positioned at the mean node coordinates in the graph.

The algorithm modeled spatial relations between two IUs when it identified the following label scheme: a locative pictorial element (a first IU), a spatial term (spatial preposition or action verb) and a referential pictorial element (a second IU). An arrow was modeled between the two IUs nodes when they were linked verbally by a spatial term depicting their spatial relation. The arrows of the graph were further classified according to the type of spatial terms label annotated (spatial prepositions in red, action verbs in blue and both in orange). This enabled graphically to represent a participant's spatial descriptions of the CTP picture.

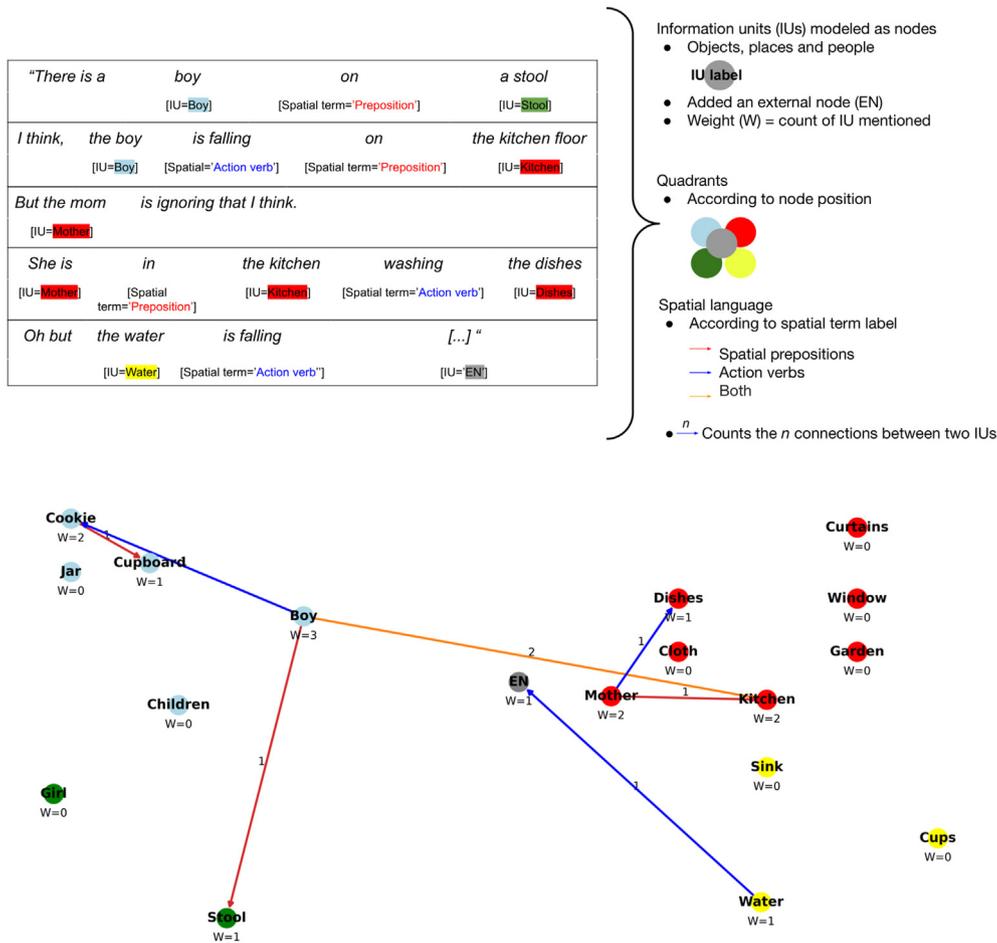


Fig. 2 – The Spatial Description Model. The description example is in English for understanding purposes. The transcribed description of the Cookie Theft Picture (CTP) task is labeled according to a list of Information Units (IUs) (the different pictorial elements in the picture) and spatial language (spatial prepositions and action verbs). The Spatial Description Model identifies which IUs are connected by spatial terms. It models the spatial relation on the graph, where the predisposed nodes are the representation of the IUs. If a spatial relation is identified, an arrow is modeled between the nodes. A weight (W) is added to the node, counting the number of times that IU is involved in a spatial relation. Each node is color coded according to its quadrant position of the picture it is in (top-left = light blue; top-right = red; bottom-left = green; bottom-right = yellow; virtual quadrant = grey). Arrows are color coded according to the type of spatial language used (spatial prepositions in red; action verbs in blue, both in orange) and counted (n). Graph features can then be extracted. Virtual quadrant (VQ).

2.3.4. Spatial graph features

Once descriptions were transformed into graphs, we extracted different graph features to assess spatial disturbances, inspired from Ambadi et al. (2021) (Table 1). We distinguished the occurrence of the node depiction in a spatial relation (weight +1 each time) whichever the eventual repetitions of a spatial relation (labeled as Node). We also assessed the occurrence of all nodes depicted excluding repetitions of the spatial relation (labeled Unique node) which corresponds to the proportion of IUs that have been spatially described. General node information gave insight on both the average node position (Average x and Average y) and the distribution of nodes across reflecting spatial exploration (Standard deviation (SD) x, SD y). Other measures assessed eventual perseverative behavior, defined as an uncontrolled repetition

of a response (Gillen & Rubio, 2016). Such behavior may appear at the node level with a participant locked on describing repeatedly a node according to itself (Selfcycle) or at the quadrant level, through spatial descriptions confined to the same quadrant (Quadrant selfcycle) or inversely by measured by the crossing ratio which consists in shifts between quadrants (Quadrant cross ratio).

To grasp quantitative spatial information at the node and overall spatial descriptions graph level, we included measures of spatial connectivity between the IUs:

- To measure the distance covered by overall spatial relations between IUs within the task (Total path distance),
- The average distance between two specific spatially described IUs (Total path distance/Unique nodes).

Table 1 – Spatial description Model's graph features.

Graph features	Measurement	Interpretation
Nodes	Number of nodes mentioned (weight ≥ 1) with eventual repetitions	The number of times a participant describes an IU's spatial relation in their narrative. This includes repeated mentions of the same IU reflecting their occurrence with spatial context and with repetitions. A high node number indicates that many IUs are described with spatial context.
Unique nodes	Number of nodes mentioned (weight ≥ 1) without repetitions	The number of times a participant describes an IU's spatial relation, however not counting the repeated mentioned of the same IU. This reflects the how many IUs (out of 18 IUs) occurred with spatial context.
Average x	Average x position of all nodes with a weight ≥ 1 in pixels	A high unique node count indicates a rich spatial description of the different IUs on the picture. The average horizontal node position of mentioned IUs describing a spatial relation. This reflects the average horizontal spatial focus of a CTP description. (0,0) is the top left corner of the CTP. Repeated IUs are counted.
Average y	Average y position of all nodes with a weight ≥ 1 in pixels	The average vertical node position of mentioned IUs describing a spatial relation. This reflects the average vertical spatial focus of a CTP description (0,0) is the top left corner of the CTP. Repeated IUs are counted.
SD x	Standard deviation of x positions of all nodes with a weight ≥ 1 in pixels	This reflects how widely spread are all spatially described objects on the horizontal axis and spatial exploration. A small SD x denotes a less dispersed spatial description, and a more concentrated spatial exploration.
SD y	Standard deviation of y positions of all mentioned nodes with a weight ≥ 1 in pixels	This reflects how widely spread are all spatially described objects on the vertical axis and spatial exploration. A small SD y denotes a less dispersed spatial description, and a more concentrated spatial exploration.
Selfcycle	Number of consecutive occurrence of a node	The number of times a participant mentions the same IU consecutively when making spatial descriptions. This assesses perseverance at the node level. A high selfcycle indicates perseverance from the participant in describing the spatial relation of the IU repetitively.
Quadrant selfcycles	Number of edge connecting nodes within the same quadrants	The number of times a participant spatially describes two IUs within the same quadrant. This assesses perseverance at the quadrant level. A high quadrant selfcycle indicates a perseverance in describing only spatial relations in a confined quadrant.
Quadrant cross ratio	Number of edge connecting nodes in different quadrants divided by the number of edges connecting nodes in the same quadrants (quadrant selfcycles)	This indicates the intra-quadrant ratio of all the spatial relations made by the participant. This reflects if a participant shifts quadrants often. A high ratio indicates a preference in spatially describing an IU with another IU in a different quadrant.
Total path distance	Sum of edges length in pixels	The total distance covered by the overall spatial relations between IUs in the participant's graph. This represents the sum of the relations between IUs. A too small total path distance indicates an insufficient connectivity of spatial relations and description. A too high total path distance indicates a disorganized of spatial relation and description.
Total path distance/ Unique nodes	Total path distance divided by the number of unique nodes	The average distance between two spatially described IUs across the participants graph, without accounting for repeated mention of the same IU. This enable to reflect the how close are the spatially described IUs. A low total path distance/unique node ratio indicates an average small distance between two spatially described IUs.

(continued on next page)

Table 1 – (continued)

Graph features	Measurement	Interpretation
Density	Ratio between edges present in a graph over maximum edges possible	This ratio is an indicator of overall spatial connections. It reflects whether spatial descriptions of IUs are dense and sparse when modeled. A low density denotes reduced spatial connectivity between IUs, hence a reduced number of spatial relations.
Reciprocity	Fraction of reciprocal edges over total edge count	The likelihood of having bidirectional relations between IUs in a graph. This reflects if two IUs are often spatially described according to each other.
Average clustering	Average of nodes fraction of triangles that actually exist over all possible triangles in its neighborhood	A low reciprocity indicates a decreased likelihood of having bi-directional spatial relations. A measure of the degree of how nodes of graph tend to cluster together. This reflects the degree of which an IU is described according to the 2 closest IUs. A low number indicates no tendency in clustering.
The Cookie Theft Picture (CTP) Information Units (IUs) are represented by the nodes in the graph; Node's weights reflect the number of times an IU is mentioned to describe a spatial relation. Spatial terms between IUs are characterized by edges in the graph. Standard Deviation (SD). Adapted from Ambadi et al., 2021 .		

- The density of the produced graph which is the number of depicted relations between nodes by the participant over the number of all possible relations in the task (Density)
- The number of bidirectional relations between IUs over the total number of relations between these IUs whatever the direction (Reciprocity).
- The likelihood of describing an IU according to its two closest IUs nodes (Average clustering).

The Spatial description graph script is available on https://gitlab.cognitive-ml.fr/lchenain/spatial_feature, and suited for python integrated development environments.

2.4. Statistical analysis

2.4.1. Spatial Description Model graph features

The graph features extracted were normalized using z-scores to account for normal distribution and homoscedasticity. Group differences were assessed with ANCOVAs controlling for sex, age, education, and unique node count. Post-hoc analyses were performed with Scheffe's test designed to determine significant group difference after an analysis of variance, hence relying on critical value of the maximum F-statistic of the ANCOVAs. It controls for family wise error rate (probability of making a Type I error when conducting multiple comparisons). It is particularly adapted after ANCOVAs that compare small sample sizes or imbalanced data sets as in our study ([Agbangba et al., 2024](#)).

2.4.2. Convergence and divergence validity

Convergence and divergence validity was performed with a correlation analysis evaluating the significant variables with cognitive measures (the SelfCog© ([Lunven et al., 2023](#))). The Total Information Coefficient estimator (TICe) and the Maximal Information Coefficient estimator (MICE) were used with minepy to measure the strength of linear and non-linear associations ([Albanese et al., 2013](#); [Reshef et al., 2016](#)). This correlation method addresses the typical challenges faced during analysis. First, it increased statistical power by decreasing the probability of making a type II error when rejecting the null hypothesis. It also can rank the associations by relationship strength no matter the type of association, also known as equitability. Lastly, it aims to resolve multiple-comparison issues. The TICe allows to screen for variables thanks to its higher power, but lower equitability, while the MICE estimates the strength of the associations because of its high equitability but lower power.

2.4.3. Post-hoc analysis: linear regressions

Evaluation of the association between the Spatial Description Model (density and SD x), disease severity measures (DBS and cUHDRS), and functional scores (UHDRS Functional Assessment Scale) was performed with univariate linear regressions in HD and preHD.

2.5. Comparison with previous language-based CTP approaches

To assess the interest of the spatial selectivity of the Spatial Description Model we compared its performance with the

previously developed language-based CTP spatial approaches issued from Alzheimer's disease on HD, preHD, and HC's CTP descriptions. We performed the spatial terms frequency analysis of spatial prepositions and action verbs (Bosse, 2019), spatial neglect analysis focusing on attention, concentration, repetition and perception (Masrani, 2018), and the Spatio-semantic graph model characterizing the descriptions' visual narrative path (Ambadi et al., 2021). The three methodological approaches are described in the Supplementary Methods (Appendix I. Supplementary Methods, Supplementary Tables 1–2), comparing HD with preHD and HC.

3. Results

3.1. Demographic and clinical assessments

The demographics and clinical scores of participants are summarized in Table 2. An ANOVA revealed no significant differences in age and years of education. As expected, significant differences were found for the TFC, Functional Assessment Scale, TMS, cUHDRS, Letter fluency (1 min), Categorical fluency (over 1 min), SDMT, Stroop color, word, and interference. Post-hoc analysis using Tukey's test revealed poorest performance in HD individuals compared to preHD and HC individuals. Fig. 3 presents the SelfCog's subtests and

average scores. ANCOVAs and post hoc analysis using Tukey's test revealed for each subtests poorer performance in HD individuals compared to preHD, and HC individuals.

3.2. Spatial Description Model graph features

The ANCOVAs determined the effect of group categories after controlling for age, education, sex, and unique nodes for graph features (Table 3). SD x , reflecting how widely spread the mentioned IUs are on the horizontal axis, was lower in HD ($\bar{x} = 109.5 \pm 9.1$) than in preHD ($\bar{x} = 112.8 \pm 9.8$) and HC ($\bar{x} = 113.2 \pm 7.9$) with $F(2, 94) = 6.527$, p -value = .002. Scheffe's test confirmed that HD's participants description of spatial representations was less dispersed than in controls (difference (d) = - .41, p -value <.05), but that preHD performed similarly than controls and HD (respectively $d = -.04$, p -value = .990, and $d = .36$, p -value = .380). Density, a measure of graphs' connectivity between the nodes, was also reduced in HD ($\bar{x} = .026 \pm .011$), compared to preHD ($\bar{x} = .028 \pm .009$) and HC ($\bar{x} = .030 \pm .006$) with $F(2, 94) = 6.887$, p -value = .002 as confirmed by the Scheffe's test (HD/HC $d = -.38$, p -value <.005), without any difference in preHD vs HC and HD (respectively $d = -.13$, p -value = .914; $d = .25$, p -value = .636). All other graph measures were similar among groups as detailed in Table 3 (all F -statistics (2,94) ≥ 2 and p -values $\geq .1$).

Table 2 – Participants' demographic and clinical assessment.

	Participants			Group comparison		Post hoc
	HD (=59) 32 F/27 M	preHD (=19) 8 F/11 M	HC (=25) 13 F/12 M	F	p-value	
Age (years)	52.7 ± 11.2	48.6 ± 12.7	54.1 ± 8.3	$F(2.0, 100.0) = 1.498$.228	
Education (years)	13.5 ± 3.4	14.7 ± 3.9	13.2 ± 3.6	$F(2.0, 98.0) = 1.115$.332	
CAG	43.8 ± 3.3	41.7 ± 2.3				
DBS	415.2 ± 96.7	286.3 ± 65.2		$F(1.0, 76.0) = 29.300$	<.001***	HD > preHD
Estimated onset (years)		6.3 ± 9.7				
TFC	10.5 ± 2.1	13.0 ± .0	13.0 ± .0	$F(2.0, 99.0) = 31.008$	<.001***	HC > HD preHD > HD
Functional Assessment Scale	21.25 ± 3.73	25 ± .0	25 ± .0	$F(2.0, 97.0) = 21.52$	<.001***	HC > HD preHD > HD
TMS	33.0 ± 15.6	.7 ± 1.3	.5 ± 1.1	$F(2.0, 99.0) = 91.14$	<.001***	HD > HC HD > preHD
Letter fluency (1min)	23.0 ± 10.1	42.2 ± 11.2	40.8 ± 11.9	$F(2.0, 100.0) = 36.658$	<.001***	HC > HD preHD > HD
SDMT	26.3 ± 10.5	51.5 ± 12.1	49.8 ± 8.3	$F(2.0, 100.0) = 69.367$	<.001***	HC > HD preHD > HD
Stroop color	47.5 ± 15.3	75.1 ± 11.1	76.7 ± 9.7	$F(2.0, 99.0) = 56.561$	<.001***	HC > HD preHD > HD
Stroop word	64.5 ± 20.2	97.9 ± 13.9	99.7 ± 10.8	$F(2.0, 99.0) = 49.836$	<.001***	HC > HD preHD > HD
Stroop interference	26.1 ± 10.3	44.4 ± 10.4	46.3 ± 8.3	$F(2.0, 99.0) = 48.567$	<.001***	HC > HD preHD > HD
Categorical fluency (1min)	12.8 ± 5.5	19.8 ± 4.6	19.1 ± 4.5	$F(2.0, 78.0) = 16.202$	<.001***	HC > HD preHD > HD
cUHDRS	9.6 ± 3.5	16.9 ± 1.5	16.9 ± 1.1	$F(2.0, 98.0) = 84.748$	<.001***	HC > HD preHD > HD

Demographic and clinical assessments of healthy control participants (HC), premanifest Huntington's Disease (preHD) and Huntington's Disease participants (HD). Worst clinical and cognitive performances are characterized by high number of CAG repeats (CAG), Disease Burden Score (DBS) and Total Motor Score (TMS) and low Functional Assessment Scale, Letter fluency (1 min), Symbol Digit Modality Test (SDMT), Stroop color, Stroop word, Stroop inferences, Categorical fluency (1 min) and composite Unified Huntington's Disease Rating Scale (cUHDRS) scores (Butters et al., 1986; Huntington Study Group, 1996; Jensen, 1965; Smith, 1982; Strauss et al., 2006). preHD is defined by a TMS <5 and a Total Functional Capacity (TFC) = 13. preHD's estimated onset predicts the years until HD's motor onset (Langbehn et al., 2004). As preHD and HC performed similarly regarding spatial language, only differences between HD and preHD or HC were presented here. Unless specified otherwise mean ± standard deviations. Male (M); Female (F). p -value<.001: ***; p -value<.01: **; p -value<.05: *.

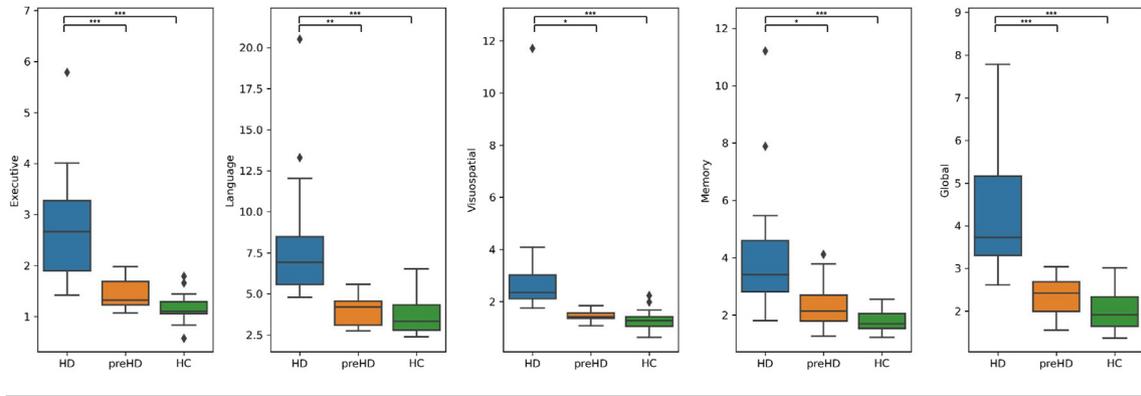


Fig. 3 – SelfCog Inverse Efficiency Score Boxplot. A high score indicates a lower cognitive performance for Inverse Efficiency Scores of the SelfCog. Huntington's Disease participants (HD), premanifest Huntington's Disease (preHD), Healthy controls (HC). p-value<.001: *; p-value<.01: **; p-value<.05: *.**

3.3. Convergence and divergence correlation analysis

The correlation analysis displayed the MICE and compared TICe, Spearman and Pearson coefficients between the HD participants that completed the SelfCog with the significant Spatial Description graph features (Table 4). The spatial measure of density correlated with the SelfCog Visuospatial component (MICE = .725, TICe p-value = .036) with both negative Pearson (R = -.208) and Spearman correlation (-.346). Density also correlated with the SelfCog Language component (MICE = .7110, TICe p-value = .050) with both negative Pearson (R = -.134) and Spearman correlation (-.310) (Fig. 4). None of the other SelfCog measures correlated with Spatial Description density or SD x measurements, namely the executive, memory and average components, with all TICe p-values ≥ .05 and MICE ≤ .65.

3.4. Post-hoc analyses

Linear regression showed that gene-carriers' density performance was associated with the UHDRS Functional Assessment Scale (coefficient (β) = 1.28, p-value = .002), with the DBS (β = -30.11, p-value = .011), and with the cUHDRS (β = 2.05, p-value ≤ .001). SD x was also associated with the cUHDRS (β = 1.78, p-value ≤ .001) but not with the UHDRS Functional Assessment Scale (β = .78, p-value = .069), nor with the DBS (β = -20.64, p-value = .086) (see Appendix 2. Supplementary Figs. 1–6).

3.5. Replication of previous methods

Previous language-based CTP approaches' results are displayed in Appendix 2. Supplementary Results (Supplementary

Table 3 – Spatial description model graph summary and group comparison.

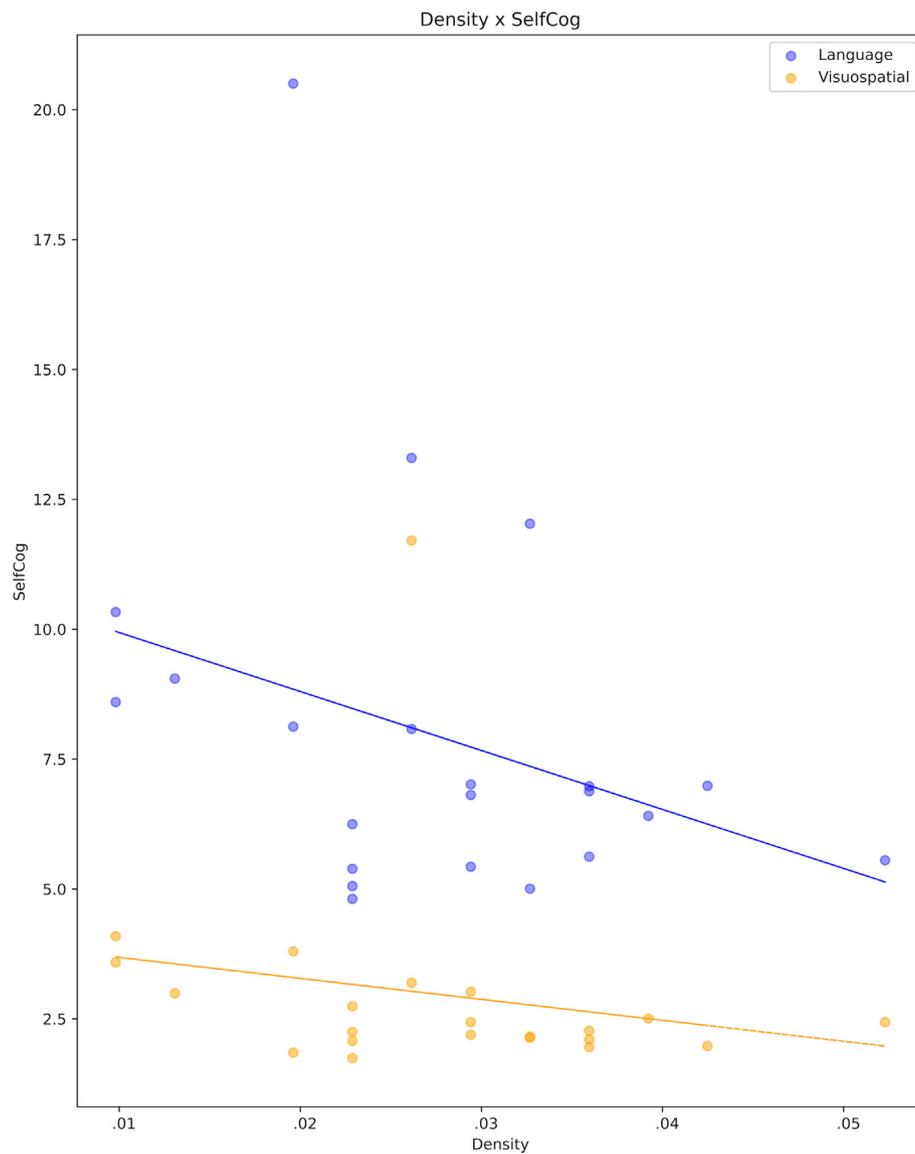
	HD	preHD	HC	F	p-value
Average x	121.7 ± 39.7 (41.2–255.5)	126.1 ± 25.5 (100.4–192.8)	125.3 ± 37.1 (70.2–240.8)	F(2.0,94.0) = .17	.844
SD x	109.5 ± 9.1 (79.7–130.0)	112.8 ± 9.8 (96.7–137.9)	113.2 ± 7.9 (99.3–132.6)	F(2.0,94.0) = 6.527	.002**
Average y	80.3 ± 25.5 (28.6–149.4)	83.8 ± 16.6 (65.6–130.8)	85.3 ± 25.0 (51.8–169.1)	F(2.0,94.0) = .209	.812
SD y	62.7 ± 11.7 (11.3–77.0)	67.4 ± 4.1 (58.3–76.1)	64.2 ± 7.0 (35.7–71.6)	F(2.0,94.0) = 1.72	.185
Total path distance	1573.4 ± 692.0 (380.1–2929.5)	1713.1 ± 651.1 (715.9–3653.4)	1797.6 ± 810.7 (550.3–3423.4)	F(2.0,94.0) = 2.038	.136
Total path distance/ Unique nodes	171.0 ± 65.8 (51.0–354.6)	163.6 ± 36.7 (79.5–228.3)	171.4 ± 57.9 (91.7–260.8)	F(2.0,94.0) = .206	.814
Nodes	21.4 ± 9.0 (4.0–50.0)	21.7 ± 7.1 (10.0–36.0)	22.2 ± 8.9 (8.0–46.0)	F(2.0,94.0) = .509	.603
Selfcycle	.4 ± .7 (.0–3.0)	.1 ± .3 (.0–1.0)	.4 ± .6 (.0–2.0)	F(2.0,94.0) = 1.409	.250
Quadrant selfcyle	3.2 ± 2.1 (.0–11.0)	3.5 ± 1.7 (1.0–7.0)	3.6 ± 1.6 (1.0–8.0)	F(2.0,94.0) = 1.862	.161
Quadrant Cross ratio	1.9 ± 1.4 (.0–7.0)	2.0 ± 1.6 (.7–8.0)	1.8 ± 1.0 (.4–5.0)	F(2.0,94.0) = .173	.841
Density	.026 ± .011 (.007–.059)	.028 ± .009 (.016–.042)	.030 ± .009 (.013–.049)	F(2.0,94.0) = 6.887	.002**
Reciprocity	.023 ± .079 (.0–.4)	.019 ± .058 (.0–.2)	.006 ± .031 (.0–.154)	F(2.0,94.0) = .494	.612
Average Clustering	.012 ± .028 (.0–.102)	.012 ± .02 (.0–.046)	.014 ± .027 (.0–.1)	F(2.0,94.0) = .068	.934

Unless specified otherwise mean ± standard deviation (min - max). Huntington's Disease participants (HD); premanifest Huntington's Disease (preHD); Healthy control participants (HC); Standard deviation of x position of all mentioned nodes (SD x); Standard deviation of y position of all mentioned nodes (SD y). p-value<.001: ***; p-value<.01: **; p-value<.05: *.

Table 4 – Correlation of significant spatial description graph features with SelfCog inverse efficiency score.

Spatial Feature	SelfCog	TICe p-value	MICe	Pearson R	Spearman ρ	Measure of non linearity
Density	Executive	.275	.395	-.453	-.365	.189
	Language	.050*	.711	-.134	-.31	.693
	Memory	.383	.516	-.135	-.147	.498
	Visuospatial	.036*	.725	-.208	-.346	.682
	Average	.144	.57	-.18	-.359	.537
SD x	Executive	.098	.519	-.096	-.102	.509
	Language	.174	.626	.208	.011	.582
	Memory	.916	.432	.113	.017	.420
	Visuospatial	.875	.273	-.158	.021	.249
	Average	.756	.342	.146	-.014	.321

Standard deviation of x position of all mentioned nodes (SD x); Maximum information coefficient estimator (MICe); Total information coefficient estimator (TICe). p-value<.001: ***; p-value<.01: **, p-value<.05: *.

**Fig. 4 – Huntington's Disease Density Score and SelfCog Language and Visuospatial Inverse Efficiency Score. A high score indicates a lower cognitive performance for Inverse Efficiency Scores of the SelfCog.**

Tables 4–6). The analyses in HD, preHD, and HC did not yield any significant results in any of the approaches demonstrating similar ratio of spatial terms, spatial neglect, and Spatio-semantic graphs.

4. Discussion

In this study, we assessed how language conveyed spatial impairments in HD by analyzing graphical representations of spoken language production of the Cookie Theft Picture task (CTP) focusing on spatial relations. We developed the Spatial Description Model in which spatial descriptions were graphically represented as a network or nodes and arrows between pictorial elements (IUs) depicted using spatial terms. In contrast with other language-based CTP approaches developed in Alzheimer's disease who failed to find any difference between HD and controls, our Model showed that language can grasp spatial abilities in manifest HD. Spatial descriptions of individuals with manifest HD expressed fewer spatial relations and less spatial exploration than both preHD and healthy controls. The convergent validity of our Model was excellent: lower graph performances in HD were solely associated with the visuospatial and language cognitive scores. The lack of association with memory or executive performances supported its divergence validity. This provides a proof-of-concept that language can capture spatial impairment in HD, paving the way for its eventual application in clinical practice.

The study provided substantial evidence for showing that spatial language reflects both spatial abilities and linguistic processing, as in healthy individuals (Bowerman et al., 1995; Dessalegn & Landau, 2013; Markostamou & Coventry, 2022; Miller et al., 2017; Rocca et al., 2020; Wallentin et al., 2007). Typically this has been demonstrated by presenting to participants experimentally controlled spatial relations, i.e., showing only two objects next to each when assessing spatial object locations (Coventry et al., 2014; Munnich et al., 2001) or by using unrelated spatial sentences (Wallentin et al., 2005). However, such approaches limit the understanding of the convergence of spatial and language systems to induced and forced spatial relations. In contrast, we used a spontaneous description task, enabling individuals to describe the picture based on their own judgment of the elements' salience, with a free-choice selection of spatial relations. As a result, our study supported proof-of-concept of our language-based analysis to assess spatial abilities in HD.

More specifically, the Spatial Description Model revealed that HD individuals have a narrower focus of spatial attention compared to controls or preHD when describing the picture. Their enumerated IUs were less dispersed along the horizontal axis than the ones of the other groups. One could argue that patients are perseverative and would keep locked on some IUs (Liu et al., 2023; Oosterloo et al., 2019; Read et al., 2013). Yet, we did not find any perseverative behavior like the previous studies (De Lucia et al., 2020; Rich et al., 1997). In contrast, individuals with HD are known to be impaired in scanning the picture and allocating their spatial attention, as shown by their attentional impairments in visuospatial attention (Bublak et al., 2006; Finke et al., 2006) and attention

shifting (Georgiou et al., 1996, 1997). We showed that individuals with HD are capable of naming as many pictorial elements as controls, suggesting that they can orient their spatial attention. This is consistent with Couette et al. who did not show reduced alerting capacities but a deficit in attentional disengagement from cued locations (Couette et al., 2008). This might explain their reduction of spatial attentional focus which could be related to reduced dopaminergic neurotransmission within the cortico-striatal pathway (Lawrence et al., 2000; Nieoullon, 2002). However, the reduced spatial connectivity between the depicted pictorial elements, and the reduced spatial exploration of manifest HD here might rather be attributed to the early cortical degeneration found in HD neuroimaging studies. This included parietal and temporal cortices atrophy, which are areas responsible for spatial processing, thus explaining HD's difficulties when scanning for spatial information regarding an environment (Blekher et al., 2009; Johnson et al., 2021; H. Lange, 1981; O'Rourke et al., 2011; Wolf et al., 2014). Damage to brain structures may vary from one individual to another in HD, including the parietal and temporal cortices but also the hippocampus and fronto-striatal brain circuit involved in working spatial, the last being majorly involved in cognitive dysfunction (Brandt et al., 2005; Glikmann-Johnston et al., 2019). The Spatial Description Model does not predict the brain structures affected in patients but shows sensitivity in HD pathology, where spatial disorders are not in the foreground. Presumably, the model is adaptable to other neurodegenerative pathologies with various brain damage as long as patients are able to describe orally an image. It follows the same constraints as any image description task.

In traditional HD spatial assessment, tests heavily relied on other high-order cognitive domains. For instance, visuo-constructive and visual-perceptual tasks also require motor and executive effort, while spatial navigation tasks rely on memory encoding and retrieval (Brandt et al., 2004; Lawrence et al., 2000). The use of the SelfCog allows to properly validate the psychometric properties of the Spatial Description Model as it allows comparison of several functions with similar input, output, and time procedure. We demonstrated the convergence validity by the correlation of the graph density with both the visuospatial and language tasks of the SelfCog. The former includes trials featuring visually similar but semantically unrelated objects, stimulating situations that may be encountered in a scene-dependent description tasks like the CTP. It also evaluates other components, such as different examples of the same object and object mental rotation, which are equally important for reflecting a comprehensive visuospatial assessment (Lunven et al., 2023; Mueller et al., 2018). This shows that the attentional explanation of the disturbances observed in HD with the Spatial Description Model cannot resume the whole story. Acknowledging that the visuospatial part of the SelfCog does not assess attention, this shows that patients also have proper spatial abilities impairments. In addition, the language part of the SelfCog supposes to name a picture covertly by comparing the onset of the names of the two pictures displayed on the screen. The patients' impairments in this task thus reflects their difficulty in expressing orally the spatial relations from the CTP. In contrast, the lack of correlation between the

Spatial Description performances and the motor, executive and memory parts of the SelfCog endorsed the targeted spatial language selectivity. By utilizing a picture description task, individuals engaged primarily in visual scanning, object localization, attention allocation and language abilities (Taylor & Cutsuridis, 2011). The study thus demonstrated that such a task can efficiently assess spatial abilities while limiting the involvement of other cognitive domains with an excellent divergent validity. Achieving such construct validity has been recognized as a challenge in the cognitive assessment of HD individuals. Even if numerous cognitive tests are available to assess decline, HD cognitive scales or screening tools that have met clinimetric/psychometric properties for screening, measuring severity and measuring change are scarce (Mestre et al., 2018). The construct validity of the Spatial Description Model is thus one of those, with its internal validation of spatial assessment through language for HD. Finally, spatial disturbances follow the course of the disease (cUHDRS) and are influenced by genetic factors (DBS). They correlate with patients' functional abilities (UHDRS functional rating scales), revealing their impact on their daily lives.

The dissimilarities in performance observed between Alzheimer's disease and HD may stem from the distinct cognitive profile associated with each pathology. Indeed, as we strictly compared the Spatial Description Model with the other language-based CTP spatial assessments on our HD population, we showed that our Model was sensitive in HD whereas, the spatial term frequency analysis, spatial neglect evaluation, and Spatio-semantic graph model were not. This might look surprising at first glance, but is easily explained by the contrastive pattern between patients with HD and Alzheimer's disease. Alzheimer's disease primarily affects the hippocampus, which plays an essential role in memory and navigation (Coughlan et al., 2018; Nedelska et al., 2012; Rao et al., 2022) whereas HD affects primarily the striatum and the fronto-striatal circuit (Tabrizi et al., 2019). Consequently, individuals with Alzheimer's disease encounter more impairments than HD with navigation, spatial memory and orientation difficulties, leading Alzheimer's patients to commonly get lost compared with the latter (K. W. Lange et al., 1995; Lineweaver et al., 2005; Possin, 2010; Snowden et al., 2007). In contrast, the main reported complaints in HD concern psychomotor, attention and time processing domains (Lemoine et al., 2021; Paulsen, 2011; Snowden et al., 2007). While spatial disturbances are present in HD (Coppin et al., 2018), such as mental rotation or visual scanning, they remain subtler compared to the prominent spatial impairments seen in Alzheimer's disease. Thus, the reported disorganized narrative path in Alzheimer's (Ambadi et al., 2021) and spatial neglect (Masrani, 2018) matches with their expected cognitive profile. Regarding Alzheimer's production of spatial terms, the reduced spatial prepositional frequency (Bosse, 2019) cannot bring definite evidence for a true spatial language production impairment. Indeed, CTP linguistic studies have shown older speakers' lexical content is less diverse, a cofactor which was not considered in the original study by Bosse (Ardila & Rosselli, 1996; Cho et al., 2021). Our approach also focused on the integration of action verbs, unlike any other CTP methods. This was particularly relevant in HD as patients display difficulties in verb productions along the

evolution of the condition (Péran et al., 2004; Jensen et al., 2006). We also strengthened the Model by avoiding perseverations, which might be useful in a more severe cohort of HD patients as the ones assessed here; they were presumably at a too early stage to make perseverations a problem. This might explain why the Spatial Description Model unmasked subtle defects that were not captured by the models developed in Alzheimer's disease. These results show that developing a digital and remote test using language is worth the effort, including in the space domain.

Translation to clinical practice would require the automation of voice data which implies technical challenges in HD. While the field of natural language processing (NLP) has greatly developed in the past years, it has not proved efficacy for dysarthric patients yet. The existing NLP models for dysarthric individuals rely on speaker-dependent speech features, creating a bias towards speech intelligibility (acoustic-phonetic decoding) opposed to comprehensibility (message reconstruction), limiting their generalization (Alaka & Shibwabo, 2023; Qian & Xiao, 2023). Once they will be adapted to dysarthric patients, the automation of spatial language and object annotation with an automatic verification system at the utterance level (e.g., identifying the relevant words) could be applied to our Spatial Description Model (Barbera et al., 2021) using an automatic extraction of the IUs and spatial terms. In the meantime, language models can be applied and fine-tuned on transcribed speech, as demonstrated in the automated scoring of autobiographical interviews (van Genugten & Schacter, 2024).

Some limitations should be considered for future research on spatial language and cognition using the Spatial Description Model. First, while the CTP is the worldwide picture description task reference, the design of the picture may prevent us from showing neglect impairment in HD. Despite that spatial neglect is not a characteristic of the HD population (only a case report (Ho et al., 2003)), studies have reported exaggerated left-side pseudo-neglect (Ho et al., 2004) and deficits in simultaneous object perception (Finke et al., 2006, 2007). The current study did not report these findings with the developed approach nor with spatial neglect assessment (Masrani, 2018). These discrepancies may be due to the unequal distribution of objects and actions across the CTP, which challenges their assessment. A picture description task should have a balanced spatial distribution of objects and events within the frame, which may improve diagnostic accuracy for patients with visual or attention deficits (de Vries et al., 2022). Considering the advantages of picture description tasks, including their ecological validity, easy implementation, collection and ability to elicit real-life spoken language, this encourages future applications to test the Spatial Description Model with a different picture. For example, the updated CTP developed by Miro (<http://miro.one>) (Berube et al., 2019) has equally balanced objects, making it optimal for spatial neglect assessment. Secondly, the CTP was designed to assess different degree of saliences, semantics, and causal and temporal relations (Cummings, 2019). This leads to describing the scene's objects by drawing causal relations between them, in other words, only using allocentric spatial coding of information (object-to-object). Additionally, preHD individuals performed similarly to non-carriers

presumably because their occipital atrophy is less important than manifest HD individuals (Johnson et al., 2015). Individuals transitioning from the preHD to manifest stage exhibited a highest rate of cortex volume change in the occipital regions, followed by the parietal regions (Johnson et al., 2021). Alternatively, the limited preHD cohort size could have prevented us from identifying spatial disturbances consistent with their preserved performance of preHD in the visuospatial SelfCog subtask, their normal cognitive functions measured with the cUHDRS, and other SelfCog functions. Lastly, the size of our groups was not estimated in the prospective longitudinal cohorts REPAIR-HD & BIO-HD as they were designed for developing new tools, in which the measures efficacy was unknown. Finding eligible participants and controls can be a challenge for any rare disease, making small sample size inevitable. We know higher sample sizes increase statistical power (Djulbegovic & Ioannidis, 2019; Lan et al., 2010). Still, the sample size was adequate enough to obtain differences between the group and was consistent with the size with other current HD speech studies (Riad et al., 2022; Chan et al., 2022; Kouba et al., 2018).

5. Conclusion

The Spatial Description Model presented in this study demonstrated that language can grasp spatial deficits in the context of HD, in contrast to previous language-based CTP spatial analyses (Ambadi et al., 2021; Bosse, 2019; Masrani, 2018). We graphically modeled spatial relations of HD's picture description speech production. It avoided counting non-spatial content of the picture descriptions as spatial. Our study contributes to the line of work demonstrating how speech and language is a powerful tool in HD assessments. By showing that speech can also track spatial capacity, we show that the required automatization of the Spatial Description Model assessment for easy clinical dissemination is worthwhile. This contributes to the development of a comprehensive speech approach to spatial abilities in both clinical and research settings, making patient assessment easier, digitized, and ultimately remote. This may answer some needs associated with the disease, namely limited access to appropriate healthcare systems and lengthy assessments.

Data statement

The conditions of our ethics approval which includes the ethical consent of participants, and the collected data does not allow for public archiving of anonymized study data. On reasonable request, readers seeking access to the data should contact the corresponding author. Access will be granted to named individuals in accordance with ethical procedures for the reuse of sensitive data including a research partnership and completion of a data transfer partnership by the APHP. Legal copyright restrictions prevent public archiving of the UHDRS, which can be obtained from UHDRS® | - Huntington Study Group and the SelfCog®, which can be obtain from the agence pour la protection des programmes IDDN FR 001 230010 001 S A 2020 000 31 230.

Open practices

The study's procedures and analyses were not pre-registered prior to the research being conducted. We reported how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to the data analysis, all manipulations, and all measure in the study.

CRedit authorship contribution statement

Lucie Chenain: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Rachid Riad:** Writing – review & editing, Validation, Software, Methodology, Data curation, Conceptualization. **Nicolas Fraisse:** Writing – review & editing, Resources, Investigation. **Cécilia Jubin:** Writing – review & editing, Resources, Investigation. **Graça Morgado:** Writing – review & editing, Resources, Investigation. **Katia Youssov:** Writing – review & editing, Resources, Investigation. **Marine Lunven:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **Anne-Catherine Bachoud-Levi:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors report no conflict of interest.

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Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cortex.2024.04.014>.

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