

**Title: The Cognitive Profile of Hereditary Spastic Paraplegia: A Systematic Review of the Literature**

**Journal: Neurological Sciences**

**Authors:** Alessia Quinzi<sup>1</sup>, Elettra Capogna<sup>2</sup>, Lucia Guidi<sup>1</sup>, Giovanni Rizzo<sup>3</sup>, David Neil Manners<sup>1,4</sup>, Rocco Liguori<sup>2,3</sup>, Raffaele Lodi<sup>2,5</sup>, Caterina Tonon<sup>1,2</sup>, Magali Jane Rochat<sup>1</sup>

**Authors affiliations:**

<sup>1</sup> IRCCS Institute of Neurological Sciences of Bologna, Functional and Molecular Neuroimaging Unit, Bologna, Italy

<sup>2</sup> Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy

<sup>3</sup> IRCCS Institute of Neurological Sciences of Bologna, UOC Neurological Clinic, Bologna, Italy

<sup>4</sup> Department for Life Quality Sciences, University of Bologna, Bologna, Italy

<sup>5</sup> IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy

**Corresponding author:**

Raffaele Lodi

IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy.

raffaele.lodi@unibo.it

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## 1. Search Strategy

**Database: Pubmed, Cochrane libraries, APA Psychinfo, Scopus, Web of Science**

**Date: 13/12/2023**

**Total results: 343**

### **PUBMED**

((spastic paraplegia, hereditary[MesH Terms]) AND ((neuropsychological tests[Mesh Terms]) OR (neuropsychological assessment[All fields]) OR (neuropsychological profile[All fields]) OR (neuropsychological functioning[All fields]) OR (neuropsychological exam[All fields]) OR (neuropsychological correlates[All fields]) OR (cognitive assessment[All fields]) OR (cognitive dysfunction[Mesh Terms]) OR (cognitive functioning[All fields]) OR (cognitive exam[All fields]) OR (cognitive function[All fields]) OR (cognitive profile[All fields]) OR (cognitive correlates[All fields]) OR (mental status and dementia tests[MesH Terms]) OR (memory functioning[All fields]) OR (executive functioning[All fields]) OR (executive function[All fields]) OR (frontal assessment battery[All fields]) OR (working memory[All fields]) OR (visual memory[All fields]) OR (verbal memory[All fields]) OR (visual learning[All fields]) OR (verbal learning[All fields]) OR (processing speed[All fields]) OR (attention[All fields]) OR (visuospatial functioning[All fields]) OR (visuospatial function[All fields]) OR (social cognition[All fields]) OR (theory of mind[All fields])))

**Results: 130**

### **Meshterms**

#### ➤ **NEUROPSYCHOLOGICAL TESTS – MESH TERM**

- Neuropsychological Testing
- Testing, Neuropsychological
- Tests, Neuropsychological
- Neuropsychologic Tests
- Neuropsychologic Test
- Neuropsychological Test
- Test, Neuropsychological
- Hooper Visual Organization Test
- Behavioral Assessment of Dysexecutive Syndrome
- Controlled Oral Word Association Test
- Cognitive Function Scanner
- Continuous Performance Task
- AX-CPT
- Rey-Osterrieth Complex Figure
- Clock Test
- Developmental Neuropsychological Assessment
- NEPSY
- Symbol Digit Modalities Test
- Paced Auditory Serial Addition Test
- Test of Everyday Attention
- Tower of London Test
- Cambridge Neuropsychological Test Automated Battery
- CANTAB
- Aphasia Tests
- Memory for Designs Test

- Repeatable Battery for the Assessment of Neuropsychological Status
- Delis-Kaplan Executive Function System
- Cognitive Testing
- Testing, Cognitive
- Cognitive Tests
- Cognitive Test
- Test, Cognitive
- Tests, Cognitive

#### **COGNITIVE DYSFUNCTION – MESH TERM**

- Cognitive Dysfunctions
- Dysfunction, Cognitive
- Dysfunctions, Cognitive
- Cognitive Impairments
- Cognitive Impairment
- Impairment, Cognitive
- Impairments, Cognitive
- Cognitive Disorder
- Cognitive Disorders
- Disorder, Cognitive
- Disorders, Cognitive
- Mild Cognitive Impairment
- Cognitive Impairment, Mild
- Cognitive Impairments, Mild
- Impairment, Mild Cognitive
- Impairments, Mild Cognitive
- Mild Cognitive Impairments
- Cognitive Decline
- Cognitive Declines
- Decline, Cognitive
- Declines, Cognitive
- Mental Deterioration
- Deterioration, Mental
- Deteriorations, Mental
- Mental Deteriorations

#### **MENTAL STATUS AND DEMENTIA TESTS – MESH TERM**

- Mental Status and Dementia Test
- General Practitioner Assessment of Cognition
- GPCOG
- Montreal Cognitive Assessment
- Mental Status Tests
- Mental Status Test
- Neurocognitive Tests
- Neurocognitive Test
- Neurobehavioral Cognitive Status Examination
- COGNISTAT
- Unified Parkinson's Disease Rating Scale
- UPDRS Panel
- Mini Mental State Examination
- Folstein Mini-Mental State Examination
- MMSE, Mini Mental State Examination
- Mini Mental Status Examination

- Mini-Cog
- Clinical Dementia Rating
- Clinical Dementia Rating Scale
- Dementia Rating Scale
- MicroCog
- Cognitive Assessment Screening Instrument

## **SPASTIC PARAPLEGIA, HEREDITARY – MESH TERM**

- Paraplegia, Spastic, Hereditary
- Spastic Paraplegia-Hypertrophic Motor-Sensory Neuropathy
- Spastic Paraplegia Hypertrophic Motor Sensory Neuropathy
- Hypertrophic Motor-Sensory Neuropathy-Spastic Paraplegia
- Hypertrophic Motor Sensory Neuropathy Spastic Paraplegia
- Hereditary Spastic Paraplegia
- Hereditary Spastic Paraplegias
- Paraplegia, Hereditary Spastic
- Paraplegias, Hereditary Spastic
- Spastic Paraplegias, Hereditary
- X-Linked, Spastic Paraplegia, Hereditary
- Hereditary Autosomal Dominant Spastic Paraplegia
- Autosomal Dominant Hereditary Spastic Paraplegia
- Peroneal Muscular Atrophy with Pyramidal Features, Autosomal Dominant
- Spastic Paraplegia, Hereditary, Autosomal Dominant
- Hereditary, Spastic Paraplegia, Autosomal Dominant
- Charcot-Marie-Tooth Disease with Pyramidal Features, Autosomal Dominant
- Charcot Marie Tooth Disease with Pyramidal Features, Autosomal Dominant
- Autosomal Dominant Spastic Paraplegia Hereditary
- Spastic Paraplegia, Autosomal Dominant, Hereditary
- Hereditary X-Linked Recessive Spastic Paraplegia
- Hereditary X Linked Recessive Spastic Paraplegia
- Spastic Paraplegia, Hereditary, X-Linked Recessive
- X Linked Recessive Hereditary Spastic Paraplegia
- X-linked Recessive Hereditary Spastic Paraplegia
- Spastic Paraplegia Type 2
- Spastic Paraplegia 2
- Hereditary, Spastic Paraplegia, X-Linked Recessive
- Spastic Paraplegia, X-Linked Recessive, Hereditary
- Hereditary Motor-Sensory Neuropathy with Pyramidal Signs
- Hereditary Motor Sensory Neuropathy with Pyramidal Signs
- HMSN V (Hereditary Motor and Sensory Neuropathy Type V)
- Type V Hereditary Motor and Sensory Neuropathy
- CMT with Pyramidal Features
- Hereditary Motor and Sensory Neuropathy 5
- Hereditary Motor And Sensory Neuropathy V
- HMSN V
- HMSN Type V
- Type V, HMSN
- HMSN 5
- Autosomal Recessive Hereditary Spastic Paraplegia
- Autosomal Recessive Spastic Paraplegia, Hereditary
- Spastic Paraplegia, Hereditary, Autosomal Recessive
- Hereditary Spastic Paraplegia, Autosomal Recessive
- Hereditary Autosomal Recessive Spastic Paraplegia
- Spastic Paraplegia, Autosomal Recessive, Hereditary

## COCHRANE LIBRARIES

#1 MeSH descriptor: [spastic paraplegia hereditary] explode all trees

#2 MeSH descriptor: [cognitive dysfunction] explode all trees

#3 MeSH descriptor: [neuropsychological tests] explode all trees

#4 neuropsychological assessment OR neuropsychological exam OR neuropsychological profile OR neuropsychological functioning OR neuropsychological correlates OR cognitive assessment OR cognitive exam or cognitive profile OR cognitive correlates OR cognitive functioning OR cognitive function

#5 MeSH descriptor:[Mental Status and Dementia Tests] explode all trees

#6 memory functioning OR executive functioning OR executive function OR frontal assessment battery OR working memory OR visual memory OR verbal memory OR visual learning OR verbal learning OR processing speed OR attention OR visuospatial function OR visuospatial functioning OR social cognition OR theory of mind

#7 (#1 AND #2) OR (#1 AND #3) OR (#1 AND #4) OR (#1 AND #5) OR (#1 AND #6)

**Results: 1**

## APA Psychinfo

((MA spastic paraplegia hereditary) AND ((MA neuropsychological tests) OR (TX neuropsychological assessment) OR (TX neuropsychological profile) OR (TX neuropsychological functioning) OR (TX neuropsychological exam) OR (TX neuropsychological correlates) OR (TX cognitive assessment) OR (MA cognitive dysfunction) OR (TX cognitive functioning) OR (TX cognitive exam) OR (TX cognitive function) OR (TX cognitive profile) OR (TX cognitive correlates) OR (MA mental status and dementia tests) OR (TX memory functioning) OR (TX executive functioning) OR (TX executive function) OR (TX frontal assessment battery) OR (TX working memory) OR (TX visual memory) OR (TX verbal memory) OR (TX visual learning) OR (TX verbal learning) OR (TX processing speed) OR (TX attention) OR (TX visuospatial functioning) OR (TX visuospatial function) OR (TX social cognition) OR (TX theory of mind)))

**Results: 21**

## SCOPUS

The search performed using “All fields” produced a large number of results that were not consistent with the search query, so the search field was restricted to the title, abstract and keywords of the documents.

((TITLE-ABS-KEY(spastic paraplegia hereditary) AND TITLE-ABS-KEY (cognitive dysfunction))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (neuropsychological tests))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (neuropsychological assessment))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (neuropsychological profile))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (neuropsychological functioning))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (neuropsychological exam))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (neuropsychological correlates))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (cognitive assessment))) OR ((TITLE-ABS-KEY (spastic paraplegia

hereditary) AND TITLE-ABS-KEY (cognitive functioning))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (cognitive exam))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (cognitive function))) ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (cognitive profile))) ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (cognitive correlates))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (mental status and dementia test))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (memory functioning))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (executive functioning))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (executive function))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (frontal assessment battery))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (working memory))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (visual memory))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (verbal memory))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (verbal learning))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (visual learning))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (processing speed))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (attention))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (visuospatial functioning))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (visuospatial function))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (social cognition))) OR ((TITLE-ABS-KEY (spastic paraplegia hereditary) AND TITLE-ABS-KEY (theory of mind)))

## Results: 6

## WEB OF SCIENCE

- #1 (ALL=(spastic paraplegia hereditary)) AND ALL=(neuropsychological tests) Results: 11
- #2 ((ALL=(spastic paraplegia hereditary))) AND ALL=(cognitive dysfunction) Results: 34
- #3 (ALL=(spastic paraplegia hereditary)) AND ALL=(neuropsychological assessment) Results: 13
- #4 (ALL=(spastic paraplegia hereditary)) AND ALL=(neuropsychological profile) Results: 6
- #5 (ALL=(spastic paraplegia hereditary)) AND ALL=(neuropsychological functioning) Results: 10
- #6 (ALL=(spastic paraplegia hereditary)) AND ALL=(neuropsychological exam) Results: 0
- #7 (ALL=(spastic paraplegia hereditary)) AND ALL=(neuropsychological correlates) Results: 7
- #8 (ALL=(spastic paraplegia hereditary)) AND ALL=(cognitive assessment) Results: 29
- #9 (ALL=(spastic paraplegia hereditary)) AND ALL=(cognitive functioning) Results: 51
- #10 (ALL=(spastic paraplegia hereditary)) AND ALL=(cognitive exam) Results: 0
- #11 (ALL=(spastic paraplegia hereditary)) AND ALL=(cognitive function) Results: 51
- #12 (ALL=(spastic paraplegia hereditary)) AND ALL=(cognitive profile) Results: 9
- #13 (ALL=(spastic paraplegia hereditary)) AND ALL=(cognitive correlates) Results: 15

#14 (ALL=(spastic paraplegia hereditary)) AND ALL=(mental status and dementia tests) Results: 1

#15 (ALL=(spastic paraplegia hereditary)) AND ALL=(memory functioning) Results:18

#16 (ALL=(spastic paraplegia hereditary)) AND ALL=(executive functioning) Results:14

#17 (ALL=(spastic paraplegia hereditary)) AND ALL=(executive function) Results: 14

#18 (ALL=(spastic paraplegia hereditary)) AND ALL=(frontal assessment battery) Results: 1

#19 (ALL=(spastic paraplegia hereditary)) AND ALL=(working memory) Results: 5

#20 (ALL=(spastic paraplegia hereditary)) AND ALL=(visual memory) Results: 0

#21 (ALL=(spastic paraplegia hereditary)) AND ALL=(verbal memory) Results: 6

#22 (ALL=(spastic paraplegia hereditary)) AND ALL=(verbal learning) Results: 2

#23 (ALL=(spastic paraplegia hereditary)) AND ALL=(visual learning) Results: 0

#24 (ALL=(spastic paraplegia hereditary)) AND ALL=(processing speed) Results: 4

#25 (ALL=(spastic paraplegia hereditary)) AND ALL=(attention) Results: 40

#26 (ALL=(spastic paraplegia hereditary)) AND ALL=(visuo spatial functioning) Results: 1

#27 (ALL=(spastic paraplegia hereditary)) AND ALL=(visuo spatial function) Results: 1

#28 (ALL=(spastic paraplegia hereditary)) AND ALL=(social cognition) Results: 4

#29 (ALL=(spastic paraplegia hereditary)) AND ALL=(theory of mind) Results: 0

#30 #1 OR #2 OR #3 OR #4 OR #5 OR #7 OR #8 OR #9 OR #11

Results: 99

#31 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #21 OR #22 OR #24 OR #25 OR #26 OR #27 OR #28

Results: 86

**Total results: 185**

**Supplementary Table 1** Eligibility Criteria

<b>S</b>	Sample	Individuals of any age, sex and ethnicity with a genetically confirmed diagnosis of HSP, either Pure or Complicated forms, with various type of genetic mutations.
<b>PI</b>	Phenomenon of Interest	Neuropsychological information that outlines the cognitive functioning of various HSP forms.
<b>D</b>	Design	Studies should preferably include a comparison or control group, alternatively they should compare the patients' performance with the normative data in order to be delineate healthy or pathological functioning of the investigated cognitive domain. The main outcome of the assessment should comprise the cognitive test scores or the qualitative description of patients' performance.
<b>E</b>	Evaluation	Second level-neuropsychological assessment that use batteries with multiple subtests or different tests to investigate various cognitive domains. It is assumed that using a simple screening tool or a single test score is not sufficient to outline the cognitive functioning profile of these patients
<b>R</b>	Research type	Qualitative, quantitative, and mixed or multi-methods.

The Sample, Phenomena of Interest, Design, Evaluation, Research type (SPIDER) tool was used to design the review. SPIDER is appropriate for systematic reviews with qualitative and multi-methods research questions [1]

**Supplementary Table 2** Cognitive domains assessed and overview of neuropsychological tests

<b>Cognitive domain / Test</b>	<b>Study reference</b>
<b>Global cognitive functioning</b>	<b>N = 27 studies</b>
Mini mental state examination (MMSE)	Agosta et al. (2015), Chamard et al. (2016), Duning et al. (2010), Goizet et al. (2009), Hsu et al. (2022), Jacinto-Scudeiro et al. (2019), Kim et al. (2009), Ribai et al. (2008), Scuderi et al. (2009), Soares et al. (2021), Tallaksen et al. (2003), Wang et al. (2022), Zhang et al. (2017)
Cambridge Cognitive Examination (CAMCOG)	Byrne et al. (2000), McMonagle et al. (2004; 2006), Murphy et al. (2009), Orlacchio et al. (2005; 2008), Tallaksen et al. (2003), Webb et al. (1998)
Montreal Cognitive Assessment (MoCA)	Hocquel et al. (2022), Jacinto-Scudeiro et al. (2019), Rattay et al. (2020), Soares et al. (2021), Utz et al. (2022), Wang et al. (2022)
Mental Deterioration Battery (MDB)	Carosi et al. (2015)
Clinical Dementia Rating (CDR)	Wang et al. (2022)

Short Test of Mental Status (STMS)	Webb et al. (1998)
Brief Neuropsychological Inventory (ENB2)	Martinuzzi et al. (2016)
Brief Cognitive Screening Battery (BCSB)	Soares et al. (2021)
Cambridge Neuropsychological Test Automated Battery (CANTAB)	Rattay et al. (2020)
Addenbrooke's Cognitive Examination (ACE-R)	Faber et al. (2018)
Mattis Dementia Rating Scale	Ribaï et al. (2008)
Florida Mental Status Examination (FMSE)	Zhang et al. (2017)
<b>Intelligence</b>	<b>N = 11 studies</b>
Wechsler Adult Intelligence Scale (WAIS) / Wechsler Intelligence Scale for Children (WISC)	Erichsen et al. (2009), Hsu et al. (2022), Lupo et al. (2020), Martinuzzi et al. (2016), Scheuer et al. (2005), Scuderi et al. (2009), Siri et al. (2010), Svenstrup et al. (2010), Webb et al. (1998)
Raven's Colored Progressive Matrices (CPM)	Agosta et al. (2015), Lupo et al. (2020), Scuderi et al. (2009), Svenstrup et al. (2010)
DART/ NART / SGWRT	Nielsen et al. (2004), Scheuer et al. (2005), Webb et al. (1998)
<b>Language</b>	<b>N = 9 studies</b>
Boston Naming Test	Siri et al. (2010), Wang et al. (2022), Zhang et al. (2017)
BADA (short version)	Lupo et al. (2020)
Visual/ Picture Naming Test	Chamard et al. (2016), Hsu et al. (2022)
Token test	Martinuzzi et al. (2016), Siri et al. (2010)
Peabody picture vocabulary test	Siri et al. (2010)
DO80	Hocquel et al. (2022)
Aural Comprehension Test	Hsu et al. (2022)
Sentence Generation	Scheuer et al. (2005)
<b>Executive functions</b>	<b>N = 20 studies</b>
Verbal Fluency (phonological + semantic)	Agosta et al. (2015), Duning et al. (2010), Erichsen et al. (2009), Hocquel et al. (2022), Hsu et al. (2022), Jacinto-Scudeiro et al. (2019), Kim et al. (2009), Lupo et al. (2020), Martinuzzi et al. (2016), Siri et al. (2010), Soares et al. (2021), Svenstrup et al. (2010), Utz et al. (2022), Wang et al. (2022), Webb et al. (1998), Zhang et al. (2017)
Wisconsin Card Sorting Test (WCST) / Modified Card Sorting Test (MCST)	Chamard et al. (2016), Lupo et al. (2020), Hsu et al. (2022), Scheuer et al. (2005), Siri et al. (2010), Svenstrup et al. (2010), Webb et al. (1998)
Stroop test	Erichsen et al. (2009), Hocquel et al. (2022), Kim et al. (2009), Lupo et al. (2020), Svenstrup et al. (2010), Wang et al. (2022)
Frontal Assessment Battery (FAB)	Goizet et al. (2009), Hocquel et al. (2022), Ribaï et al. (2008), Soares et al. (2021)
Tower of London (TOL)	Lupo et al. (2020), Siri et al. (2010), Utz et al. (2022)
Paced Auditory Serial Addition Task (PASAT)	Agosta et al. (2015), Erichsen et al. (2009)
Color Word Interference Test (CWIT)	Duning et al. (2010)
Continuous subtraction	Svenstrup et al. (2010)

Proverb interpretation (RH battery)	Scheuer et al. (2005)
Isaacs Set Test (RAPID battery)	Chamard et al. (2016)
Cognitive estimation	Martinuzzi et al. (2016), Utz et al. (2022)
First-edge-palm test (FEP)	Zhang et al. (2017)
<b>Memory</b>	<b>N = 20 studies</b>
<b>Verbal Memory</b>	<b>N= 19 studies</b>
Digit Span	Agosta et al. (2015), Chamard et al. (2016), Erichsen et al. (2009), Hocquel et al. (2022), Lupo et al. (2020), Martinuzzi et al. (2016), Nielsen et al. (2004), Scheuer et al. (2005), Siri et al. (2010), Svenstrup et al. (2010), Utz et al. (2022), Wang et al. (2022), Zhang et al. (2017)
Rey's Auditory Verbal Learning Test (RAVLT)	Jacinto-Scudeiro et al. (2019), Kim et al. (2009), Lupo et al. (2020), Wang et al. (2022)
California Verbal Learning Test (CVLT) / Auditory Verbal Learning Test (ALVT)	Duning et al. (2010), Erichsen et al. (2009), Zhang et al. (2017)
Wechsler Memory Scale (WMS)	Duning et al. (2010), Hsu et al. (2022), Scheuer et al. (2005), Scuderi et al. (2009), Utz et al. (2022), Webb et al. (1998)
Memory prose / Rivermead Behavioural Memory Test (RBMT story)	Agosta et al. (2015), Lupo et al. (2020), Martinuzzi et al. (2016), Utz et al. (2022)
Free and Cue Selective Recall Test (FCSRT)	Chamard et al. (2016), Hocquel et al. (2022)
Paired associates learning (RH Battery)	Scheuer et al. (2005)
Sentence repetition (RH Battery)	Scheuer et al. (2005)
Luria memory words test	Siri et al. (2010)
Fuld Object Memory	Webb et al. (1998)
<b>Visual memory</b>	<b>N= 11 studies</b>
Corsi/visuospatial Span	Agosta et al. (2015), Chamard et al. (2016), Lupo et al. (2020), Siri et al. (2010)
Rey's Complex Figure – recall	Agosta et al. (2015), Duning et al. (2010), Erichsen et al. (2009), Martinuzzi et al. (2016), Lupo et al. (2020), Siri et al. (2010), Svenstrup et al. (2010), Wang et al. (2022)
Continuous Visual Memory Test (CVMT)	Erichsen et al. (2009)
Door test	Goizet et al. (2009)
Beehive Visual Memory test	Chamard et al. (2016)
Pattern recognition task	Utz et al. (2022)
<b>Visuoperception</b>	<b>N = 5 studies</b>
Benton	Hocquel et al. (2022), Webb et al. (1998)
Street	Scheuer et al. (2005)
Navon	Zhang et al. (2017)
Tangled figures (ENB-2)	Martinuzzi et al. (2016)
<b>Visuoconstruction</b>	<b>N = 10 studies</b>
Rey Complex Figure - copy	Agosta et al. (2015), Duning et al. (2010), Erichsen et al. (2009), Lupo et al. (2020), Martinuzzi et al. (2016), Siri et al. (2010), Svenstrup et al. (2010), Wang et al. (2022)
Copy of Drawings (with and without landmarks)	Martinuzzi et al. (2016)
Clock Drawing Test	Martinuzzi et al. (2016), Soares et al. (2021)

Block Design (RH battery)	Scheuer et al. (2005)
<b>Attention</b>	<b>N = 15 studies</b>
Trail making test (TMT)	Agosta et al. (2015), Chamard et al. (2016), Duning et al. (2010), Hocquel et al. (2022), Hsu et al. (2022), Martinuzzi et al. (2016), Nielsen et al. (2004), Scheuer et al. (2005), Siri et al. (2010), Svenstrup et al. (2010)
Symbol Digit Modalities Test (SDMT) /Digit symbol	Duning et al. (2010), Scheuer et al. (2005), Svenstrup et al. (2010), Webb et al. (1998)
2 and 7 selective attention test / selective attention and interference test	Erichsen et al. (2009), Utz et al. (2022)
Multiple Features Target Cancellation (MFTC)	Lupo et al. (2020)
Test of Attentional Performance (TAP)	Chamard et al. (2016)
Cancellation and Line bisection test	Zhang et al. (2017)
<b>Social cognition</b>	<b>N = 5 studies</b>
Social cognition and emotional assessment (SEA)	Chamard et al. (2016), Hocquel et al. (2022)
The emotion attribution test (EA)	Lupo et al. (2020)
Reading the Mind in the Eyes Test (RME)	Lupo et al. (2020)
The Theory of Mind task (ToM task)	Lupo et al. (2020)
Cerebellar Cognitive Affective Syndrome Scale (CCAS)	Lupo et al. (2020), Soares et al. (2021)
Florida Affective Battery	Zhang et al. (2017)
<b>Visual-motor skills</b>	<b>N = 4 studies</b>
Purdue Pegboard	Hsu et al. (2022), Webb et al. (1998)
Visual motor integration (VMI)	Siri et al. (2010)
Visual gestalt (RH Battery)	Scheuer et al. (2005)
<b>Apraxia</b>	<b>N = 2 study</b>
Batterie breve d'évaluation des praxies gestuelle /Praxis test	Hocquel et al. (2022), Martinuzzi et al. (2016)

**Supplementary Table 3** Quality assessment for all quantitative studies (n = 20) using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies (EPHPP) [2]

Authors (year)	A) Selection Bias				B) Study design			C) Confounders				D) Blinding			E) Data Collection				F) Withdrawals and Drop-out				Global Index	Global Rating
	Q1	Q2	SC	R	Rand	SC	R	Q1	Q2	SC	R	Q1	SC	R	Q1	Q2	SC	R	Q1	Q2	SC	R		
Agosta et al., 2015	1	1	1	S	NO	2	M	1	1	1	S	2	2	M	1	1	1	S	2	1	1	S	1	S
Byrne et al., 2000	1	1	1	S	NO	2	M	2		1	S	1	3	W	1	1	1	S	2	1	1	S	2	M
Duning et al., 2010	1	1	2	M	NO	2	M	3	4	3	W	1	3	W	1	1	1	S	2	1	1	S	3	W
Erichsen et al., 2009	1	1	2	M	NO	2	M	1	2	2	M	1	3	W	1	1	1	S	1	1	1	S	2	M
Faber et al., 2018	1	1	2	M	NO	2	M	1	1	1	S	1	3	W	1	1	1	S	2	1	1	S	2	M
Goizet et al., 2009	1	1	1	S	NO	3	W	1	3	3	W	1	3	W	1	1	1	S	2	1	1	S	3	W
Hsu et al., 2022	2	1	1	S	NO	2	M	3	4	3	W	1	3	W	1	1	1	S	2	1	1	S	3	W
Jacinto-Scudero et al., 2019	1	1	1	S	NO	2	M	1	4	3	W	1	3	W	1	1	1	S	2	1	1	S	3	W
Lupo et al., 2020	1	1	1	S	NO	2	M	1	1	1	S	1	3	W	1	1	1	S	2	1	1	S	2	M
Martinuzzi et al., 2016	1	1	1	S	NO	2	M	1	3	3	W	1	3	W	1	1	1	S	2	1	1	S	3	W
McMonagle et al., 2004	1	2	2	M	NO	2	M	2		1	S	1	3	W	1	1	1	S	1	1	1	S	2	M
Murphy et al., 2009	1	1	1	S	NO	2	M	1	3	3	W	1	3	W	1	1	1	S	1	1	1	S	3	W
Rattay et al., 2020	1	1	1	S	NO	2	M	1	1	1	S	1	3	W	1	1	1	S	2	1	1	S	2	M
Scheuer et al., 2005	1	1	2	M	NO	2	M	2		1	S	1	3	W	1	1	1	S	2	1	1	S	2	M
Tallaksen et al., 2003	3	1	3	W	NO	2	M	2		1	S	1	3	W	1	1	1	S	2	1	1	S	3	W
Utz et al., 2022	1	1	1	S	NO	2	M	1	1	1	S	1	3	W	1	1	1	S	2	1	1	S	2	M
Webb et al., 1998	1	2	2	M	NO	2	M	2		1	S	1	3	W	1	1	1	S	1	1	1	S	2	M

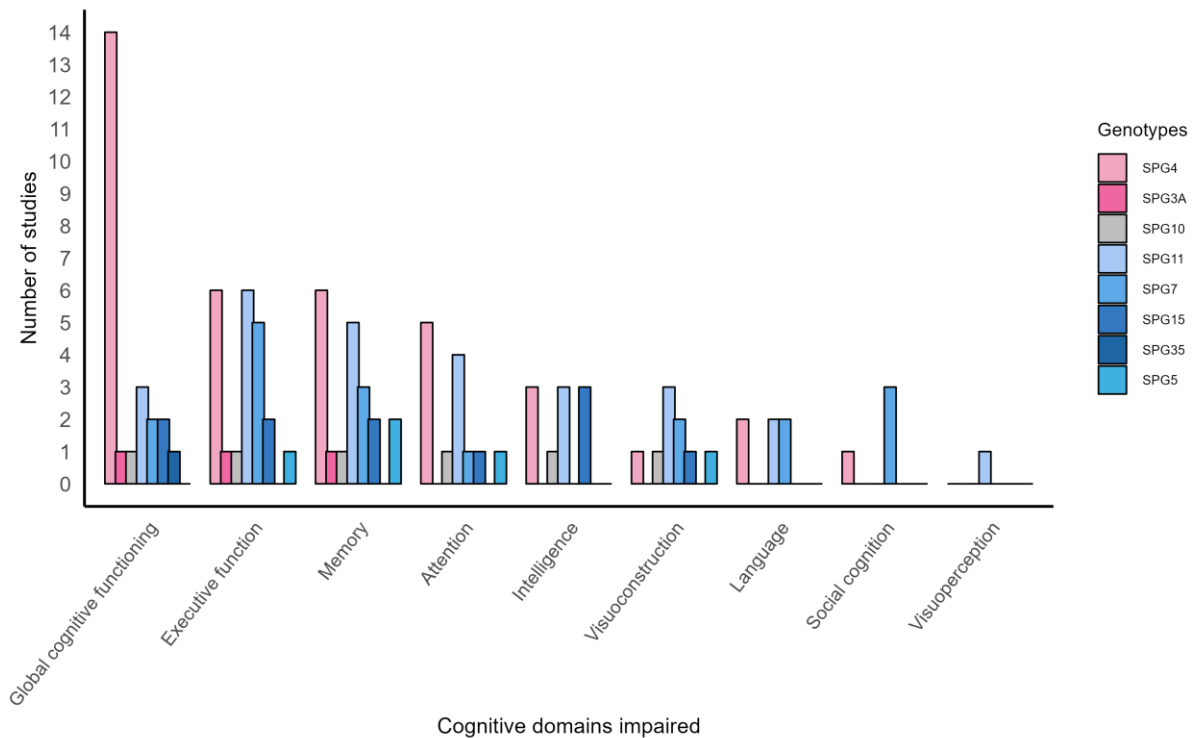
The quality of the studies included was assessed independently by two reviewers (AQ and MR) using EPHPP (Thomas et al., 2004), (<https://www.ephpp.ca/quality-assessment-tool-for-quantitative-studies/>), following the component (A-F) ratings that contribute to the global rating for each paper. SC = Score, R= Rating, Rand= Randomization, W = weak, M = moderate, S = strong

**Supplementary Table 4** Quality assessment for all case reports (n = 18) using the “CARE criteria checklist” [3]

Authors (years)	T	KW	Abstract				Intro	Patient Information				CF	TL	Diagnostic Assess				Therap Interv				Follow-up and Outcomes				Discussion				PP	Cons
	1	2	3	3	3	3	4	5	5	5	5	6	7	8	8	8	8	9	9	9	10	10	10	10	11	11	11	11	12	13	
			a	b	c	d		a	b	c	d			a	b	c	d	a	b	c	a	b	c	d	a	b	c	d			
Carosi et al., 2015	N	N	N	N	N	N	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Chamard et al., 2016	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Hocquel et al., 2022	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Kim et al., 2009	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y	
McMonagle et al., 2006	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Nielsen et al., 2004	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Orlacchio et al., 2005	N	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Orlacchio et al., 2008	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Ribai et al., 2008	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Scuderi et al., 2009	N	N	Y	N	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Siri et al., 2010	N	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	-		
Soares et al., 2021	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	N	N	N	N	Y	Y	Y	Y	N	-		
Svenstrup et al., 2010	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Wang et al., 2022	Y	Y	Y	N	N	N	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y		
Zhang et al., 2017	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	N	Y		

The quality of the studies included was assessed independently by two reviewers (AQ and MR) using CARE (Gagnier et al., 2013). T = Title, KW = Keywords, Intro = Introduction, CF= Clinical Finding, TL = Timeline, Diagnostic Assess = Diagnostic assessment, Therap Interv = Therapeutic Intervention, PP = Patient Perspective, Cons = Consent, Y = yes, N = no.

**Supplementary Fig. 1** Cognitive disorders identified in HSP genotypes



Cognitive disorders identified by the included studies for each HSP genotypes. HSP = hereditary spastic paraplegia, SPG = spastic paraplegia genes.

**References**

- 1.Cooke A.; Smith D.; Booth A. Beyond PICO: the SPIDER tool for qualitative evidence synthesis. *Qual Health Res.* **2012**, *Oct;22(10)*: 1435-43. doi: 10.1177/1049732312452938. Epub 2012 Jul 24. PMID: 22829486
- 2.Thomas, B.H.; Ciliska, D.; Dobbins, M.; Micucci, S. A Process for Systematically Reviewing the Literature: Providing the Research Evidence for Public Health Nursing Interventions. *Worldviews Evid Based Nurs* **2004**, *1*, 176-184, doi: 10.1111/j.1524-475X.2004.04006.x.
- 3.Gagnier, J.J.; Kienle, G.; Altman, D.G.; Moher, D.; Sox, H.; Riley, D.; CARE Group\* The CARE Guidelines: Consensus-Based Clinical Case Reporting Guideline Development. *Glob Adv Health Med* **2013**, *2*, 38-43, doi: 10.7453/gahmj.2013.008.