The evolution of cognitive neuropsychology: Examples from patient studies of reading disorders.

Professor Randi Starrfelt

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La Sapienza – 3/5-2018

Cognitive neuroscience

UNIVERSITY OF COPENHAGEN

Next time

Monday May 7th 10.30-13-30: Workshop on methodology: Experimental design and control, control groups, and single case statistics.

1) Revisit discussion points missed on previous seminars (day 1 and 2)
2) Task in class - group assignment: Select a cognitive function that may be affected following brain injury. Find a research question that can be addressed using a single case approach. Discuss possible ways to address this question (experimental setup). Brief group presentation during class.

Please consider point 2 before this class

Please bring a LAPTOP if you have one.

Suggested readings for today:

Starrfelt, R. (2007). Selective alexia and agraphia sparing numbers-a case study. *Brain and Language, 102*, 52-63.

Starrfelt, R., Habekost, T., & Gerlach, C. (2010). Visual processing in pure alexia: A case study. *Cortex, 46*, 242-255.

Starrfelt, R., Habekost, T., & Leff, A. P. (2009). Too little, too late: reduced visual span and speed characterize pure alexia. *Cerebral Cortex, 19*, 2880-2890.

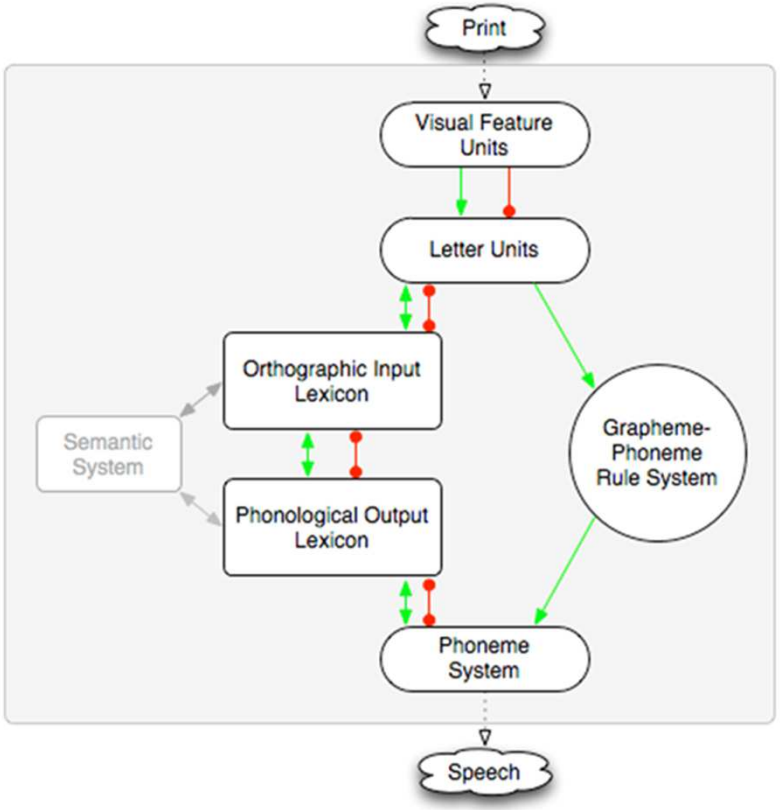
Starrfelt, R., & Behrmann, M. (2011). Number reading in pure alexia—A review. *Neuropsychologia, 49*, 2283-2298.

....Also read the papers from April 26th:

From last time

- Marshall & Newcombe (1973): Error analysis. No normal controls, but patients showed *differential deficits* (error patterns).

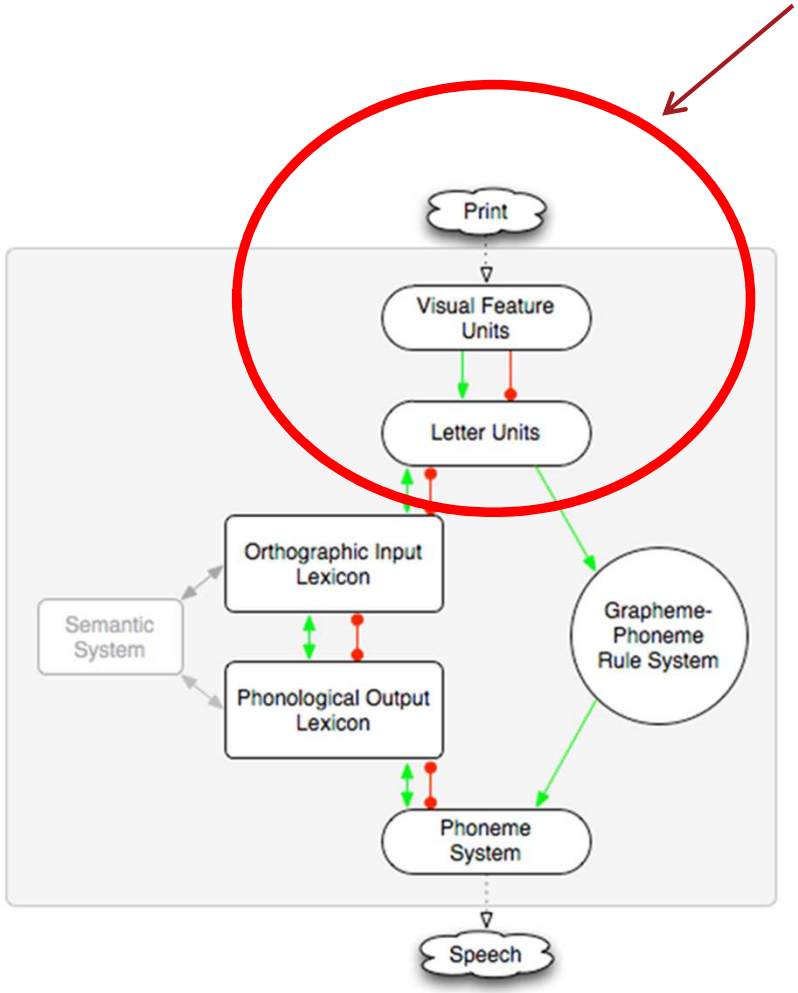
- Together with data on phonological alexia, a double dissociation between lexical and sublexcial reading was suggested.



Alexia in cognitive neuropsychology

Central	Peripheral
Deep alexia / dyslexia	Pure alexia
Surface alexia	Neglect alexia
Phonological alexia	Attentional alexia

Shallice & Warrington, 1980



Peripheral/"prelexical" effects of:

Visual field	Hemianopic alexia
Visual attention (spatial)	Neglect alexia
Visual attention (selective)	Attentional alexia
Visual (word) form perception	Pure alexia

Warrington & Shallice (1980): Word form dyslexia

- Two patients with reading deficits: JDC following glioma; RAV following intracranial haemorrhage.

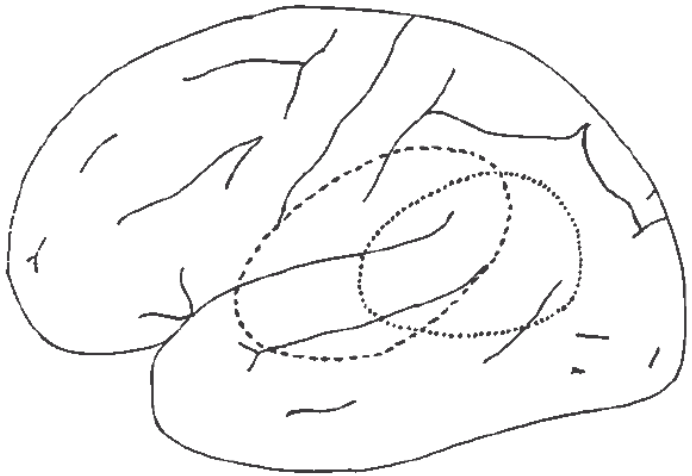
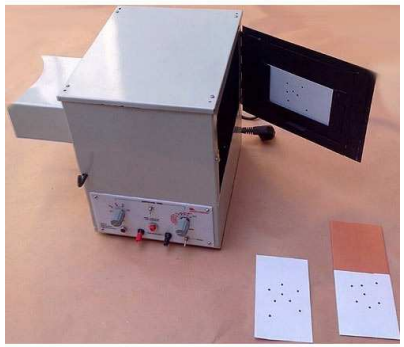


FIG. 1. Schematic diagram of location of lesions. R.A.V. .....; J.D.C. ---------.

Tested on a range of visual and language tasks, including tachistoscopic presentation



Warrington & Shallice (1980)

SUMMARY

In this study we have reported our investigations of two patients with an acquired dyslexia characterized by letter-by-letter reading, whole word reading being apparently impossible. It has been shown that this phenomenon of letter-by-letter reading cannot be accounted for by visual or perceptual factors nor by impairment of visual span of apprehension. The exceptionally slow speed of reading was documented and a clear relationship between word length and reading speed established. Performance on tasks considered to maximize whole word reading which at the same time prevent the possibility of letter-by-letter reading, namely, reading script and reading with tachistoscopic presentation, was impaired. The satisfactory performance of these two patients on tasks of picture interpretation suggests that the two components of the syndrome simultanagnosia, letter-by-letter reading and piecemeal perception of complex scenes, are dissociable. Three alternative explanations of letter-by-letter reading are considered and we conclude that in this type of acquired dyslexia there is damage to the system through which a visual word-form is attained.

Today's readings – a personal tour

Starrfelt, R. (2007). Selective alexia and agraphia sparing numbers-a case study. *Brain and Language, 102*, 52-63.

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The mysterious case that sparked it all

ELSEVIER

Brain and Language 102 (2007) 52–63

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Selective alexia and agraphia sparing numbers—a case study

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Available online 2 November 2006

Case JM

- Male, 19 years
- Head trauma following car accident
- Scans (CT, MRI, SPECT) show no certain lesions
- Opthalmologist:
  - Peripheral visual field defects
  - Pt. can read numbers but not letters

Neuropsych. assessment:

- Speech and comprehension normal.
- Visual recognition and construction intact.
- Reading and writing of letters impaired.
- All other tests same as premorbid level / compared to MZ-twin

	JM	KM
WAIS-subtests (raw scores)		
Vocabulary	30/80	30/80
Information	14/29	14/29
Similarities	11/26	11/26
Picture arrangement	30/36	28/36
Digit symbol	36	-
Incomplete pictures	16/21	20/21
Raven Advanced Progr. Matrices, Set I		
Scoring first response	4/12	5/12
Self corrected responses	3/12	2/12
Sum correct	7/12	7/12
Other		
Digit span forwards – raw score	8	5
Digit span backwards – raw score	8	6
Sentence repetition	16/22	16/22
Mental arithmetic	18/20	12/20
Block design, correct	12/12	12/12
Block design, time	13 sec	12 sec
Trail making test A	26 sec	-

Case JM – letters and words

Reading

- **Words**
  - Covers all but one letter, serially identifies / guesses
  - Can't read symbolic words like TV, WC, own name without resorting to this strategy

- **Letters:**
  - Identifies 12/28 capital letters (5-10 sec per letter)
  - Letter decision (letters – nonletters): 9/12
  - Letter matching at chance level.

Writing:

- 26/28 letters formed nicely when written alone
- Writes letters on top of eachother when writing words.
- Oral spelling OK
- Naming to spelling OK
- Copy: Tries to identify – then writes.

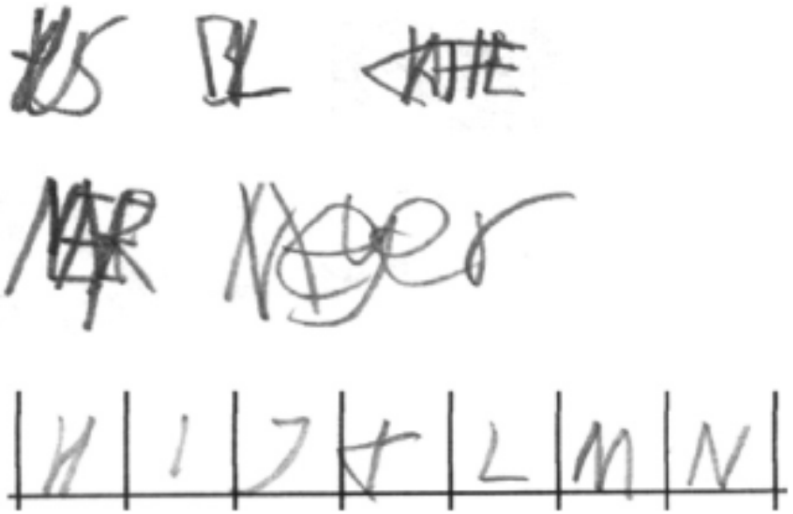
JM: numbers

Reading:

- Reads numbers up to 7 digits quickly and accurately
- Can access semantics from numbers (famous dates; magnitude etc.)

Writing:

- Number writing normal
- Written arithmetic normal



23×12

$\begin{array}{r} 36 \\ 240 \\ \hline 276 \end{array}$

809×47

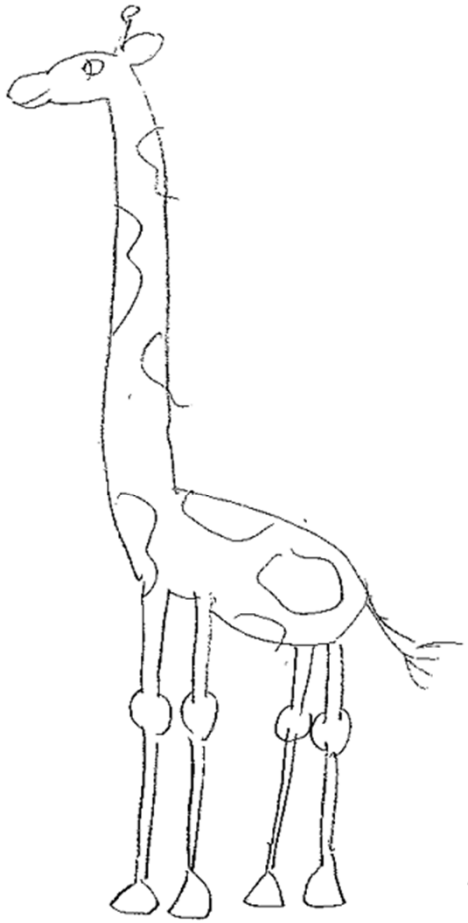
$\begin{array}{r} 5 \\ 6 \\ 423 \\ 6006 \\ 37600 \\ \hline 38023 \end{array}$

$434 : 7 = 62$

$\begin{array}{r} 42 \\ \hline 14 \\ 14 \\ \hline 0 \end{array}$

$621 : 9 = 69$

$\begin{array}{r} 541 \\ \hline 81 \\ 81 \\ \hline 0 \end{array}$



Case JM conclusion

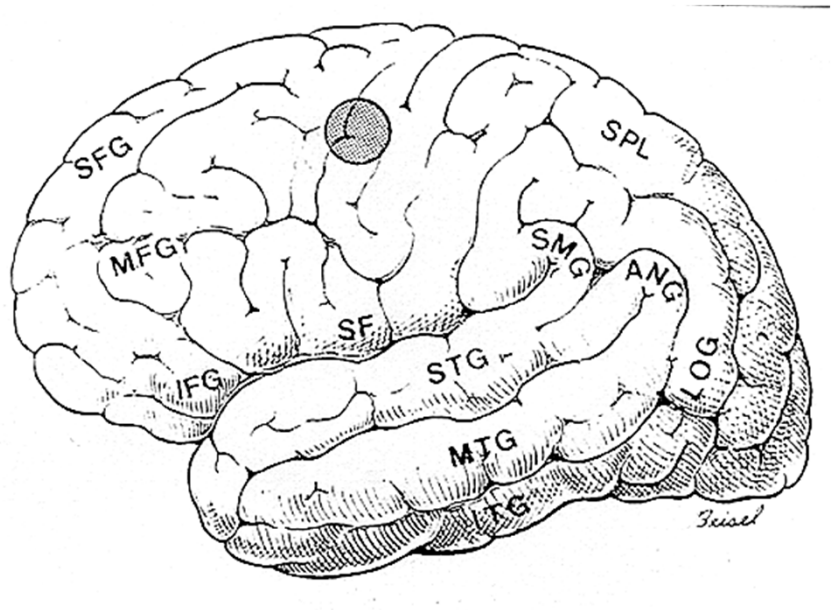
"This study shows that letter and number reading are dependent on dissociable processes."

But does it? What do you think?

Anderson et al. (Brain, 1990)

Only patient on record with same pattern of performance (impaired letters but not numbers).

Surgical lesion in Exner's area
(left premotor cortex, BA6)



So where could we go from there?

- Focal lesions in Exner's area are extremely rare (Damasio found 4/1200 patients), making it difficult to judge what role (pre) motor representations have in perception / reading based on patient studies.

- Reading of numbers rarely reported in studies of alexia, and (in 2007) never systematically investigated in a group of patients.

- The observed deficits in JM were in both recognition and production (visual and motor domain). We went on to ask whether a dissociation between letters and numbers could be found in the visual domain – in patients with pure alexia.

Pure alexia

Dejerine (1892): Monsieur C. *Alexia without agraphia.*

- Could not identify even single letters by sight
- Could write well.
- Less impaired with numbers.
- Could identify letters by writing them in his palm.

Joseph Jules Dejerine (1849-1917)

Bub, D. N., Arguin, M., & Lecours, A. R. (1993). Jules Dejerine and his interpretation of pure alexia. *Brain and Language,* 45, 531-559.

An attempt at defining pure alexia

1. Pure alexia is an **acquired reading disorder**, in previously literate subjects.

2. Such patients should show **correct writing** (spontaneously or on dictation) and normal oral spelling.

3. They should **not exhibit aphasia, dementia, or visual agnosia.**

4. They should show a **deficit in letter identification and /or word reading** (elevated RTs and a **word length effect**), or be unable to read at all.

5. Their lesions should be located in **the posterior left hemisphere.**

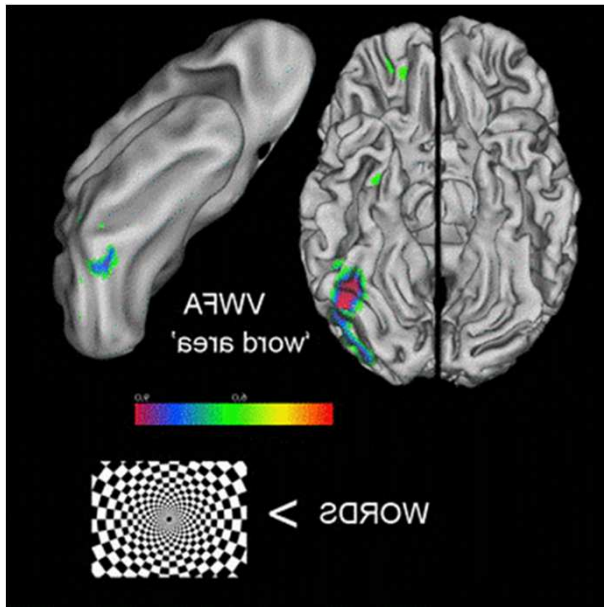
Starrfelt & Shallice (2014) *Cogntiive Neuropsychology*

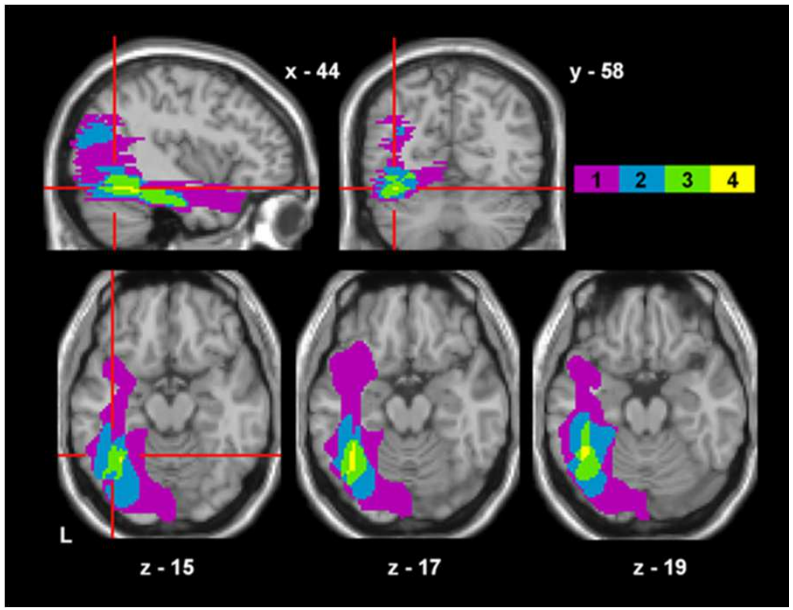
About the lesion site

- Left posterior
  - Left occipito-temporal
    - Left ventral occipito-temporal
      - Left fusiform gyrus
        - Left mid-fusiform gyrus

About the lesion site

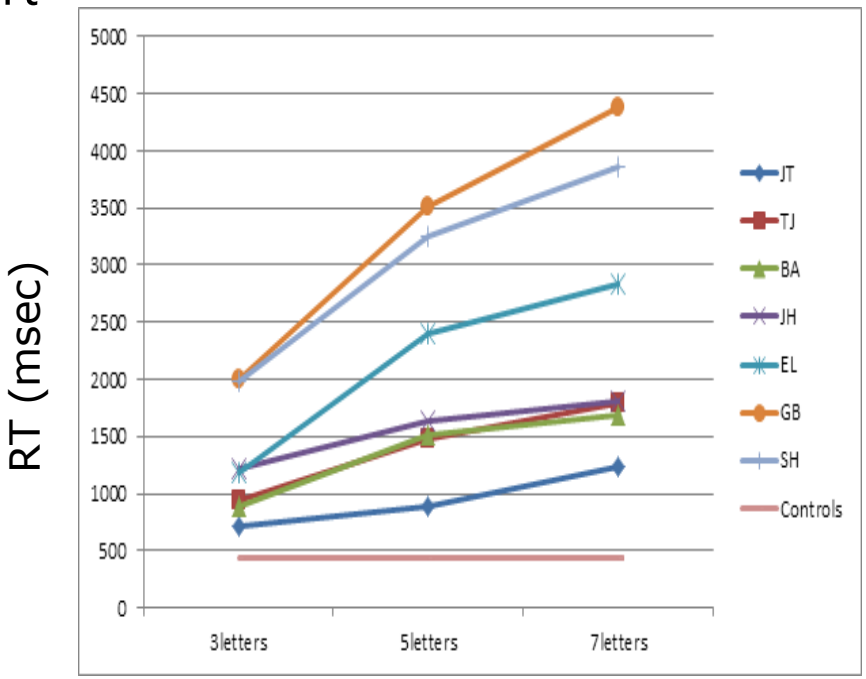
- Left posterior
  - Left occipito-temporal
    - Left ventral occipito-temporal
      - Left fusiform gyrus
        - Left mid-fusiform gyrus
          - **Visual Word Form Area (VWFA)**





Main symptom in pure alexia: Word length effect (thought to reflect letter-by-letter reading)

- LBL reading may be a conscious / overt strategy.
- May also reflect "unconscious" processing limitations.
- May arise for different reasons in different patients (e.g., hemianopic alexia and semantic dementia).
- Develops over time
- Pure alexia is the syndrome – LBL reading the (compensatory) strategy



Three main hypotheses of pure alexia

- Orthographic deficit affecting letter perception and/or visual word recognition only (Warrington & Shallice, 1980; Cohen et al.,2003; 2004).

- Visuo-perceptual deficit affecting other visual stimuli like objects, numbers/digits, simple patterns (Behrmann et al., 1998; 2009; Fiset et al., 2006; Roberts et al., 2013).

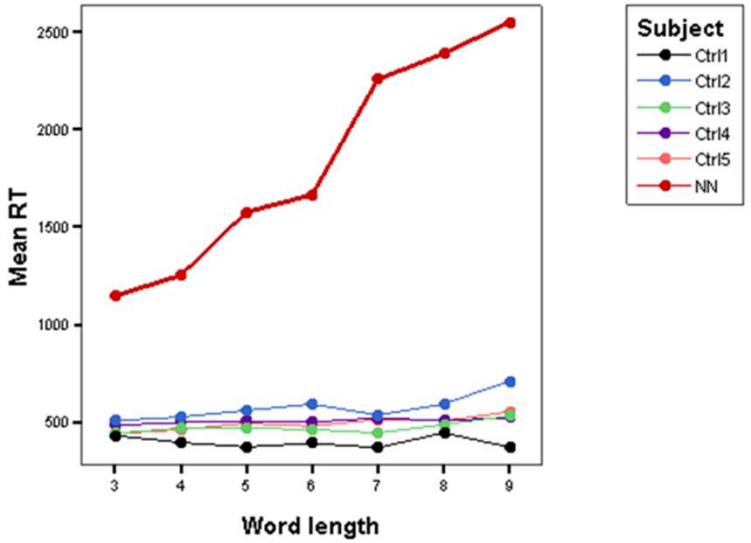
- A core deficit in simultaneous perception of multiple visual objects (Kinsbourne & Warrington, 1962; Farah, 1990; 2004).

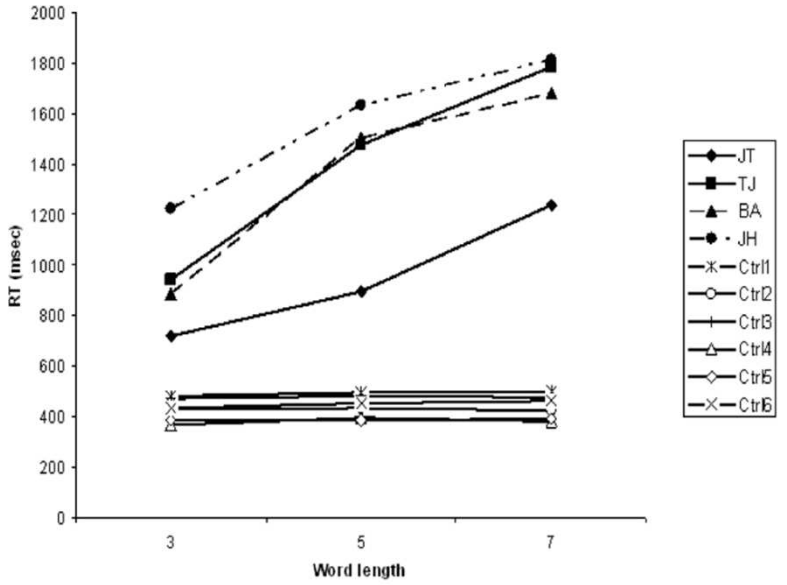
How selective is pure alexia?

- A long standing idea is that number reading can be intact in pure alexia.
- This goes back to Dejerine, who is cited as saying that number reading was normal.
- Comparing letters and numbers, then, should be the most sensitive test of the core deficit: If numbers are normal, then the deficit must be letter / orthography specific.
- Additionally, this would answer the question if a dissociation like the one displayed by JM could be found in the visual domain.

Patient studies

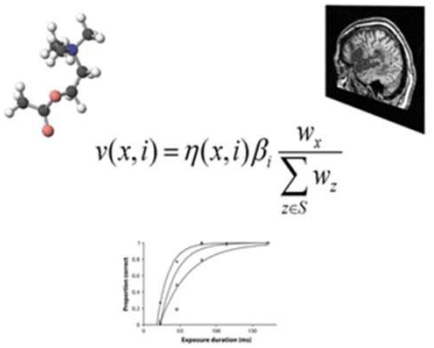
- Comparing number and letter report.
- 5 patients with (mild) pure alexia (1 DK, 4 UK) due to stroke in the posterior left hemisphere. All lesions include the putative Visual word form area (left mid fusiform gyrus).
- 10 age/education similar controls.





Starrfelt, Habekost & Leff, *Cerebral Cortex, 2009*
Starrfelt, Habekost & Gerlach, *Cortex*, 2010

Psychophysical data analysed within the framework of a Theory of Visual Attention (TVA)



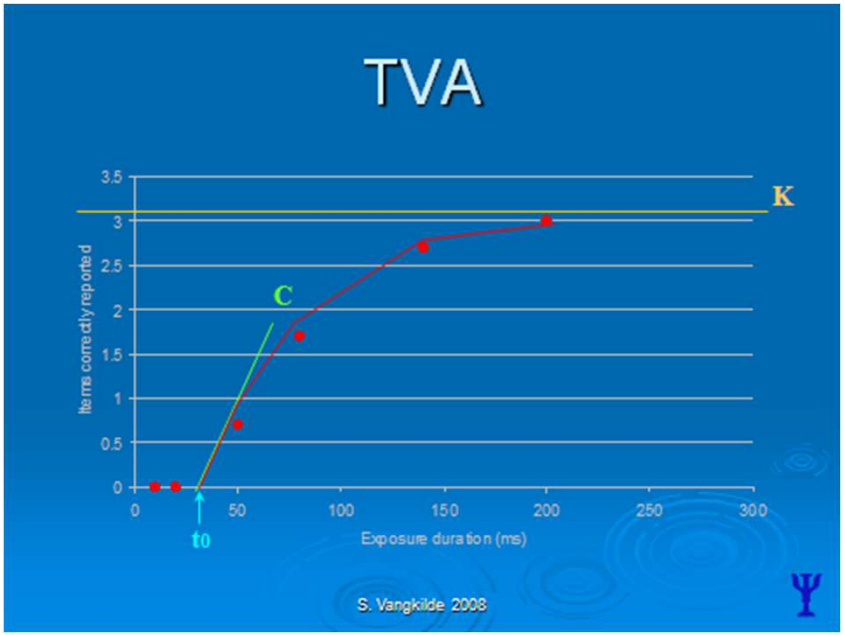
Based on relatively simple experiments, different parameters of visual attention/perception can be estimated:

- We focus on:

t0 = threshold for conscious perception (in msec)

C = speed of visual processing (items per second)

K = capacity of visual short term memory (number of items)

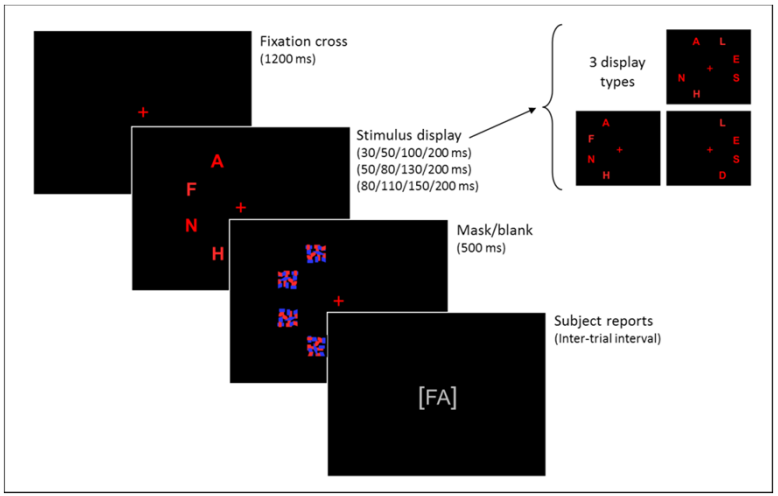


Bundesen, *Psychological Review*, 1990
Bundesen, Habkost & Kyllingbsaek, *Psych. Rev.* 2005.
Habekost, *Frontiers Psych*,, 2015: Review of clinical studies.

Psychophysical testing (brief masked exposure)

Single item report:

- Letters vs digits – central masked presentation.
- *Measures processing speed centrally.*



Whole report:

- Letters vs digits "peripheral" presentation (5 deg. from fixation).
- *Measures speed and apprehension span peripherally.*

Combining these, we can test all hypotheses at once:

Psychophysical testing of the hypotheses of pure alexia

- Orthographic deficit

  Prediction: Impaired processing speed and span for letters but not other stimuli.

- Visuo-perceptual deficit

  Prediction: Impaired processing speed and span for all stimulus types.

- Deficit in simultaneous perception

  Prediction: Reduced span for all stimulus types. Speed may be normal.

Psychophysical testing of the hypotheses of pure alexia

- Orthographic deficit

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- Visuo-perceptual deficit

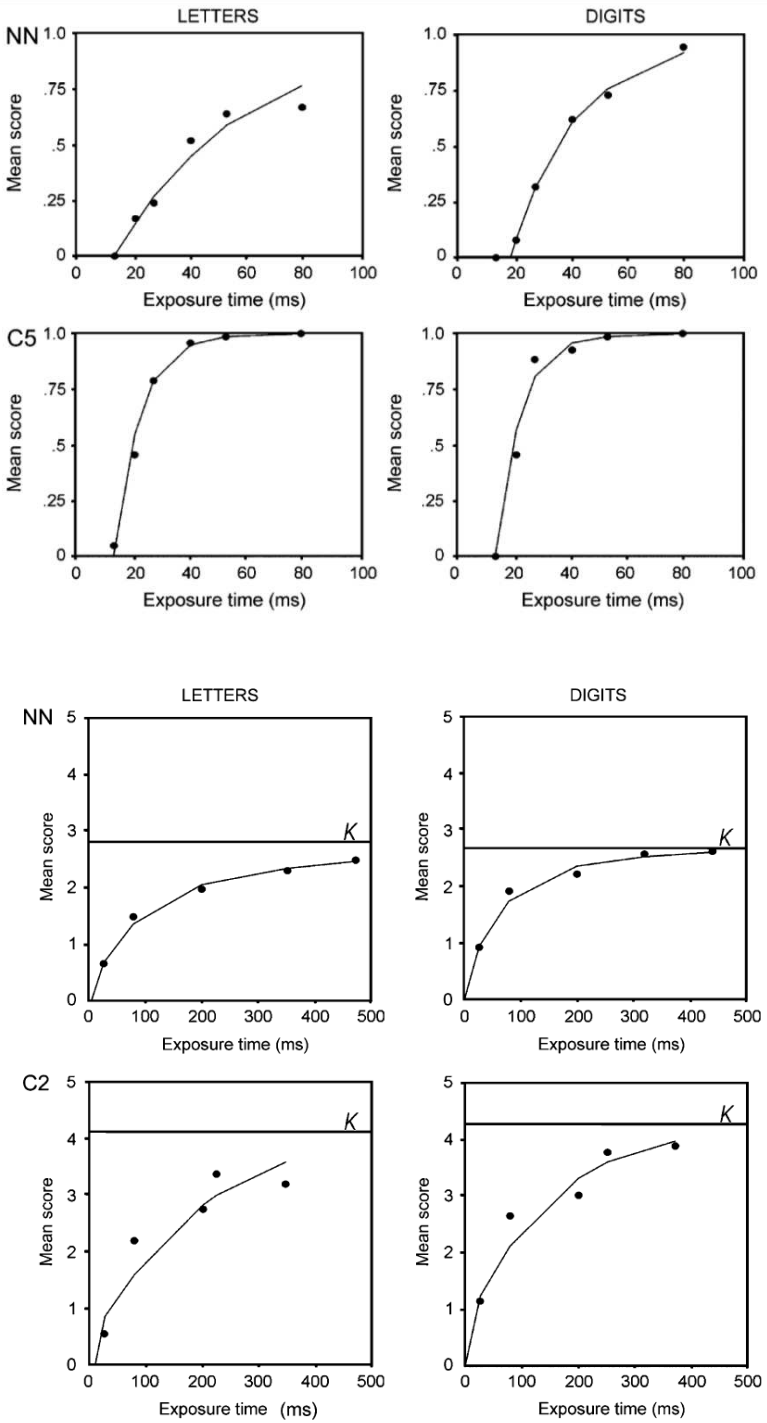
  Prediction: Impaired processing speed and span for all stimulus types.

- Deficit in simultaneous perception

  Prediction: Reduced span for all stimulus types. Speed may be normal.

The five pure alexic patients all show:

- Severely reduced processing speed for singly presented letters and digits (central presentation).
- Severely reduced visual apprehension span for letters and digits presented simultaneously (peripheral presentation).
- **No significant dissociation between performance with letters and digits.**
- Smaller (if any) difference between processing speed in central and peripheral vision.



Too little – too late

- The studied patients show reduced processing speed, and reduced processing span.
- As reading depends on **fast** processing of **many** items at once, these deficits may explain the central symptom in pure alexia – the word length effect - and possibly the general increase in reading RTs.
- Few other visual tasks make the same demands on the visual system.
- May perhaps be explained by a more 'general visual deficit' degrading all input (perhaps particularly in the central visual field).

But has number reading been shown to be intact in other patients with pure alexia?

Neuropsychologia 49 (2011) 2283–2298

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Neuropsychologia

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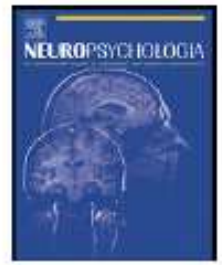


Reviews and perspectives

Number reading in pure alexia—A review

Randi Starrfelt[a,*], Marlene Behrmann[b]

[a] Center for Visual Cognition, Department of Psychology, Copenhagen University, O. Farimagsgade 2A, DK-1353 Copenhagen K, Denmark
[b] Department of Psychology, Carnegie Mellon University, Pittsburgh, PA, USA

Literature review:

- 223 studies of pure alexia (in Latin scripts) from 1892 - 2010 identified (including Dejerine's case)

•Resulting in:

- 76 papers reporting performance with numbers for 90 patients with pure alexia.
- In 46 patients, there was no difference between performance with letters and digits.
- For 28 patients, no data were presented to make an evaulation of the type of dissociation possible.
- For 5 patients tasks with letters and digits were too different for any meaningful comparison to be made.

•In the latter 33 cases, the reported pattern was better performance with digits than letters.

Remember from last time: Types of dissociations

Some established dissociations are supported by double dissociations (e.g., implicit / explicit memory; semantic / episodic memory).

In many cases, however, the dissociation only goes one way.

- Because one task is harder than another?
- Because of normal processing differences?
- Because one function is localized / modular and the other is not?

Important: The aim is to support the claim that the same pattern of performance ("dissociation") observed in the patient can not be observed in the normal population.

Types of single dissociations (Shallice, 1988)

1) Trend dissociation: Task I is performed ***markedly*** better than Task II.
   - No control group reference.

2) Strong dissociation: Neither task is performed at a normal level, but task I is performed ***very much better*** than task II.
   - Control group reference, or normals "expected to perform at ceiling level".

3) Classical dissociation: Task I is performed ***normally*** (compared to controls), performance on task II is impaired.

Quantitative / statistical criteria for 2) and 3) established by Crawford et al., e.g.,:

Crawford, J. R., Garthwaite, P. H. & Gray, C. D. (2003). Wanted: Fully operational definitions of dissociations in single-case studies. *Cortex, 39,* 357-370.

The importance of control gruops

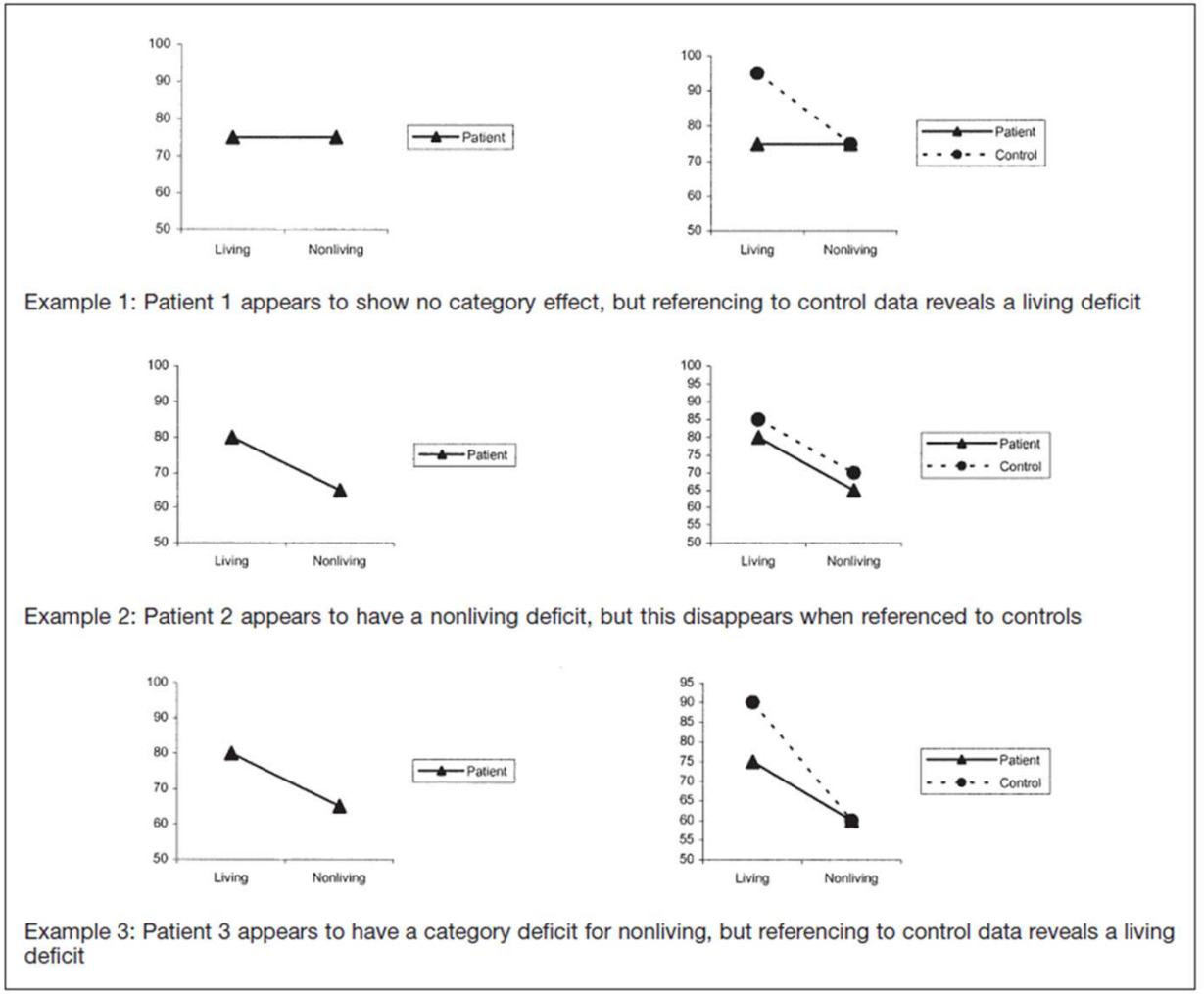
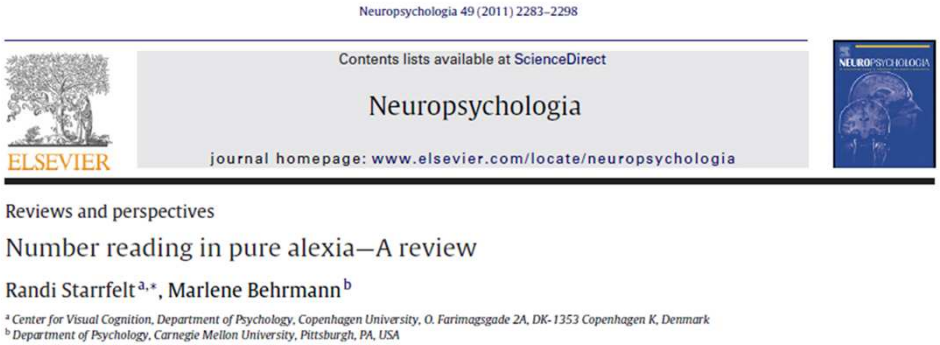


Fig. 1 – *Hypothetical examples showing how a lack of control data could distort the interpretation of category effects.*

Laws (2005)
Cortex

Trend dissociations


Neuropsychologia 49 (2011) 2283–2298

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Reviews and perspectives

Number reading in pure alexia—A review

Randi Starrfelt [a,*], Marlene Behrmann [b]

[a] Center for Visual Cognition, Department of Psychology, Copenhagen University, O. Farimagsgade 2A, DK-1353 Copenhagen K, Denmark
[b] Department of Psychology, Carnegie Mellon University, Pittsburgh, PA, USA

- 6 patients meet the qualitative criteria for a trend dissociation.
  - BUT: No control group.
    Coarse tasks
    No statistical comparisons made.

- In all these cases, the reported pattern was **better performance with digits than letters.**

Strong dissociations

- 5 patients meet the qualitative criteria for a strong dissociation:
  - **Much better performance with numbers than with letters,** with reference to a control group (or performance on the two tasks at least compared statistically).
  - Performance with numbers also impaired, but to a lesser degree.

However: Using Crawford and Garthwaite's statistical criteria for a strong dissociation, none of these results come out significant.

I.e. It cannot be concluded that the same pattern could not be observed in the normal population.

All the reported dissociations go in the same direction (numbers better than letters. So…

Is

5

just easier than

S

It seems so:

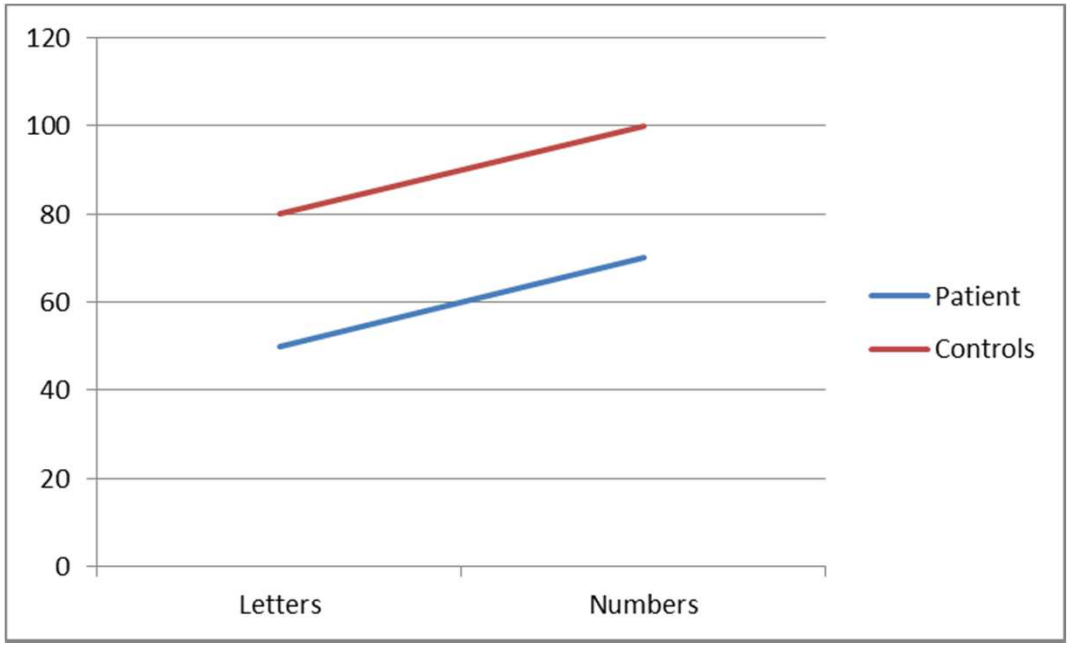
- We tested 20 students in an identification task with letters and digits, with very low exposure durations (13-53 msec, postmasked).

- Proportion correct:

Time	Digits	Letters		*t*(19)	*p*
13ms	0.39 (0.25)	0.29 (0.22)		4.3	< .001
20ms	0.74 (0.19)	0.58 (0.26)		5.6	< .001
27ms	0.91 (0.09)	0.78 (0.21)		3.5	< .01
33ms	0.95 (0.05)	0.88 (0.14)		2.8	< .02
40ms	0.97 (0.03)	0.91 (0.11)		3.0	< .01
53ms	0.98 (0.03)	0.97 (0.05)		0.77	= .454
Total	0.82 (0.10)	0.73 (0.15)		4.8	< .001

So:

- There is little (if any) evidence for dissociation between reading of letters and digits in pure alexia.
- But: There is a trend suggesting that numbers are processed better than letters.
- This pattern is also found in normal subjects.



- There is a difference – but no dissociation.

What information to look for in patient studies

- Debut (recent or stable phase?)
- Background neuropsychological measures (are there other deficits?)
- Lesion aetiology and imaging
- Diagnostic cognitive deficits and how they were measured:
  - experimental paradigm
  - test sensitivity
  - dependent variable (accuracy of reactiontimes)

- Use of control data
- Use of statistics to compare patients and controls
- Distribution of scores in controls (ceiling effects?)

- Are the conclusions of the study sufficently supported by the data (analysis)?

Just out on this topic: A classical cognitive neuropsychological study

CORTEX 101 (2018) 249–281

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

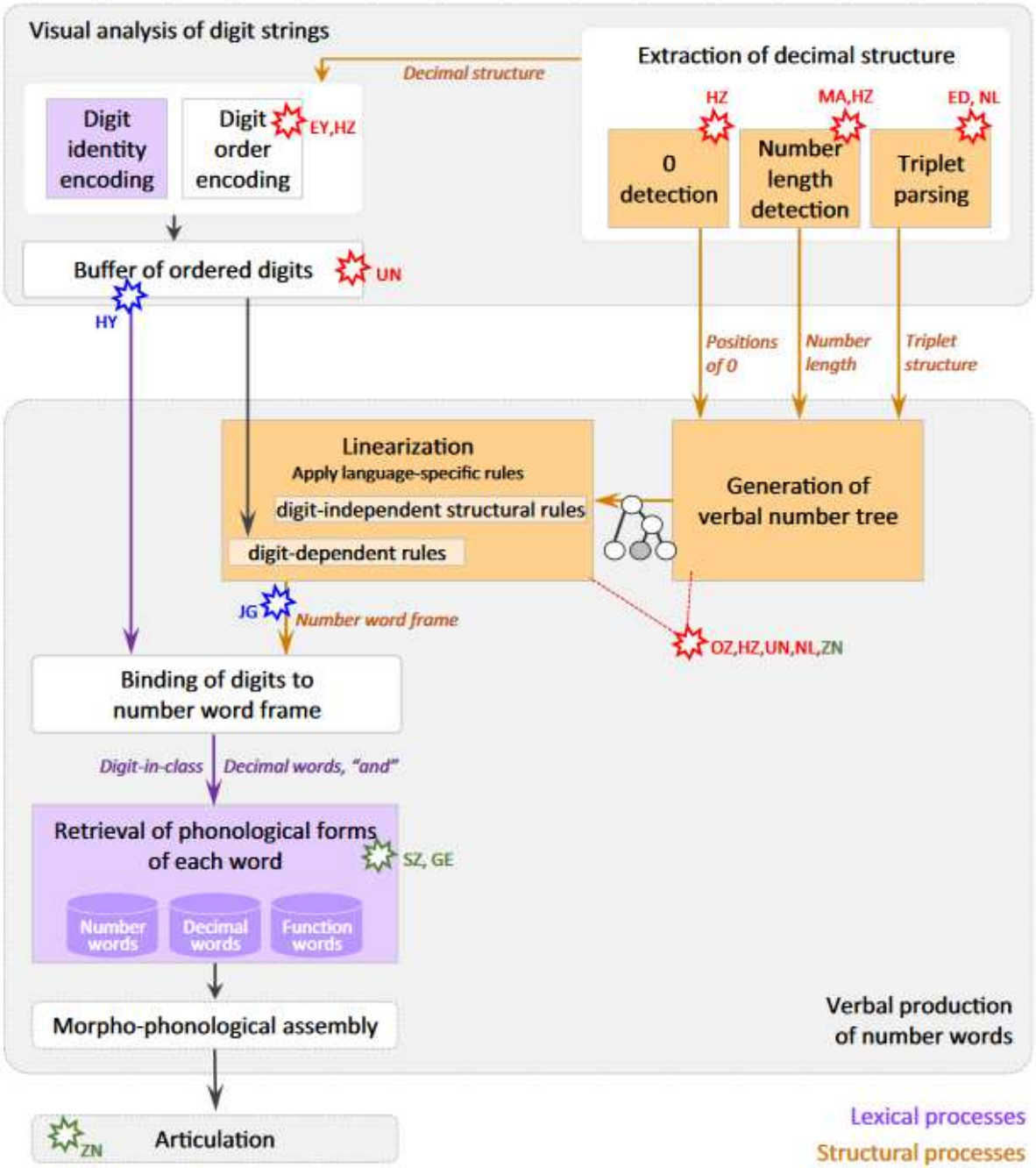
Research report

A cognitive model for multidigit number reading: Inferences from individuals with selective impairments

Dror Dotan [a,b,*] and Naama Friedmann [a]

Table 14 – The locus of deficit for each participant.

	Visual analysis					Verbal production	
	Digit identity	Digit order	Number length	0 positions	Triplet structure	Verbal structure	Phonological retrieval
EY	✓	✗	✓	✓	✓	✓	✓
HZ	✓	✗	✗	✗	?	Mild(?)	✓
MA	✓	✓	✗	?	?	✓	✓
ED	✓	✓	✓	?	✗	✓	✓
NL	✓	✓	✓	?	✗	✗	✓
OZ	✓	Mild(?)	✓	✓	✓	✗	✓
UN	✓	✓	✓	✓	✓	✗	✓


Visual analysis of digit strings
Decimal structure
Extraction of decimal structure
Digit identity encoding
Digit order encoding
EY,HZ
HZ
MA,HZ
ED, NL
0 detection
Number length detection
Triplet parsing
Buffer of ordered digits
UN
HY
Positions of 0
Number length
Triplet structure
Linearization
Apply language-specific rules
digit-independent structural rules
digit-dependent rules
Generation of verbal number tree
JG
Number word frame
OZ,HZ,UN,NL,ZN
Binding of digits to number word frame
Digit-in-class
Decimal words, "and"
Retrieval of phonological forms of each word
SZ, GE
Number words
Decimal words
Function words
Morpho-phonological assembly
Verbal production of number words
ZN
Articulation
Lexical processes
Structural processes