

Complete abolition of reading and writing ability with a third ventricle colloid cyst: implications for surgical intervention and proposed neural substrates of visual recognition and visual imaging ability.

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Complete abolition of reading and writing ability with a third ventricle colloid cyst:
Implications for surgical intervention and proposed neural substrates of visual recognition and visual imaging ability.

SUMMARY <i>Up to 150 words summarising the case presentation and outcome (this will be freely available online)</i>
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We report a rare case (DD) unable to read (alexia) and write (agraphia) after mild head injury. He had preserved speech and comprehension, could spell aloud, identify words spelled aloud and copy letter features. He was unable to visualize letters but showed no problems with digits. Neuropsychological testing revealed general visual memory, processing speed and imaging deficits. Imaging data revealed a 8mm colloid cyst of the third ventricle that splayed the fornix. Little is known about functions mediated by fornical connectivity but this region is thought to contribute to memory recall. Other regions thought to mediate letter recognition and letter imagery, Visual Word Form Area and visual pathways, were intact. We remediated reading and writing by multi-modal letter retraining. The study raises issues about the neural substrates of

reading, role of fornical tracts to selective memory in absence of other pathology, and effective remediation strategies for selective functional deficits.

BACKGROUND *Why you think this case is important – why did you write it up?*

The current case is rare in the presentation of global incapacity to read and write with no language disruption or evidence of gross pathology. We are not aware of other reported cases presenting with *global* alexia and agraphia. Patients typically present with partial alexia/agraphia and show substantial lesions to occipito-parietal regions and/or visual pathways (cf Déjèrine¹). In addition, most reported cases of colloid cysts are post-surgery because the cyst has often grown relatively large by the time the patient presents to medical services increasing intracranial pressure, compressing neural structures and requiring surgical intervention. Hence, almost all cases reported in the literature to our knowledge show secondary effects on neural structures beyond displacement of fornices due to cyst size and location or as a result of surgery, or a combination of both. These may include: Fornix transection, callosal tract disconnection, frontal atrophy, mamillary body atrophy, ventricular enlargement, hippocampal atrophy and evidence of gliosis^{2,3}. Thus, it is difficult to extrapolate the precise function of fornical tracts and surrounding structures from earlier post-surgical documented cases, and there are scant reported data revealing how a cyst abutting the fornix in an otherwise healthy brain, might disrupt cognition. The present case demonstrates severe memory dysfunction possibly as a consequence of white (fornical) matter tract disruption. Arguably, the nature of the deficit underlying memory, reading and writing deficits is visual (visual letter recognition and visual imagery ability). Findings challenge assumptions that a specific Visual Word Form Area in the brain governs reading and writing ability. Thus the case is medically rare, exceptional in the functional/clinical presentation and challenges current hypotheses regarding the neural substrates of reading/writing ability.

CASE PRESENTATION *Presenting features, medical/social/family history*

DD was aged 18 when he sustained a minor TBI (Traumatic Brain Injury) and neck injury in a road traffic accident (RTA). There was a post-traumatic amnesia of at least one hour. Accident and emergency records show that DD presented with neck injury and no loss of consciousness,

although there was a period of confusion lasting up to 5 days following the injury where DD reported loss of episodic recall for events. He was diagnosed with whiplash injuries. Imaging data showed a colloid cyst to the third ventricle abutting the fornix (see Figure 2 and 3).

DD reported that he had become progressively illiterate over a period of two months post-accident; he first became aware of it when letters on TV appeared alien ‘like foreign symbols.’ On referral he complained of inability to read or write, (although he was able to draw), memory deficits, headaches, irritation and excessive levels of fatigue on exertion. There were no clinical signs of receptive or expressive dysphasia, word finding or comprehension deficits based on screening subtests from the Test for Reception of Grammar (TROG⁴) and Psycholinguistic Assessments of Language Processing in Aphasia (PALPA⁵); social use of language appeared normal. He presented with profound inability to recognize, image or write letters based on free recall. DD was unable to recognise or write any letter (with the exception of O and X which he recognised as mathematical symbols) or words on initial interview. When words were spelled aloud he could correctly identify the word. He was unable to sign his name or write his address but could spell his name and address verbally. When asked to read a registration plate he could only read the numbers. He performed arithmetic sums presented visually. Some difficulties were noted with the spelling of exception words (sieve, dove, for example), and correctly identifying irregular words spelled aloud on a letter-by-letter basis (‘sow’ interpreted as ‘stitch’ i.e. ‘sew’). He repeated letters aloud phonetically and commented that he could not ‘see’ the letter or word ‘in his mind’s eye.’ He could recite the alphabet slowly forwards and backwards.

INVESTIGATIONS *If relevant*

DD completed a battery of measures of intelligence, memory, executive function and mood state to establish his functional profile of deficit and sparing. Test results are presented in Table one.

[Insert table 1 here]

Interpretation of test performance: General Intelligence (Wechsler Adult Intelligence Scale III⁶).

General intellectual functioning scores fell within the average range for Full-Scale, Performance and Verbal IQ indices. Conversion analyses of Verbal and Performance subtest scaled scores showed that Digit Span (SS = 6) a verbal subtest, and Digit-Symbol Coding a performance subtest scores (SS = 5) were statistically significantly lower ($p .05$) than the mean score for Verbal ($m = 11.8$) and Performance ($m = 9$) subtests overall. Although the Digit Span subtest is verbally mediated and Digit-symbol is performance based they both require manipulation of abstract symbols, which may explain DD's significantly poorer ability on these measures compared to other subtests. Vocabulary (SS = 17), Picture Completion (SS = 15) and Matrix Reasoning (SS = 13) scaled scores were statistically higher than overall Verbal and Performance means indicating excellent knowledge of the meaning of words, holistic visual processing, and problem solving with abstract visual symbols that do not have a visual structure similar to letters. The score for Verbal Comprehension Index fell within the high average range, Perceptual Organization index was Borderline, with Working Memory and Processing Speed Index scores ranging from extremely low to impaired. Verbal (110) and Performance IQ (99) scores were significantly different ($p = .05$) with DD showing poorer ability on performance compared to verbal tasks. Verbal Comprehension Index (120) score was significantly higher ($p = .05$) than Perceptual Organization Index (109), Working Memory Index (95), and Processing Speed Index scores (75). Processing Speed Index score was significantly lower than Working Memory Index score, and both were significantly lower than other Index scores ($p = .05$). His core profile indicated general working memory, information processing speed and perceptual organization weaknesses compared to verbal ability.

Visuospatial perception: Visual Object and Space Perception Battery (VOSP⁷).

DD showed intact visual perceptual and visuospatial abilities on subtests indicating that low-level perceptuo-spatial deficits were not driving poor scores on other measures.

Visual and auditory attention: the Test of Everyday Attention (TEA⁸)

DD showed impaired selective visual attention in the first minute of the task. Performance improved in the second minute falling within the borderline impaired range. He performed within

normal ranges on auditory attentional subtests (elevator counting task).

Attention and visual and verbal memory: The Attention and Memory Information Processing Battery (AMIPB⁹).

DD performed within the low average range for immediate verbal recall for the Story Recall subtest of episodic memory, and at borderline to impaired range for immediate recall for the Figure Recall subtest. He showed impaired delayed recall for verbal and visual information, and an impaired level of retention over time for both verbal and visual material on Story Recall and Figure Recall subtests (Figure 1).

[Insert Figures 1 a, b, and c here]

Figure recall drawings revealed poor retention of visual information from immediate copy with picture present to immediate and delayed copies without target stimulus present for figural features of image indicating severe disruption to visual memory.

Verbal and non-verbal visual recognition and recall: The Doors and People test¹⁰.

DD performed at the impaired range on the Doors test, a non-verbal visual recognition task and the People test, a task requiring acquisition of the name of four face stimuli across three trials. He performed at ceiling on the Shapes test requiring four simple shapes to be copied and reproduced after a delay of several seconds contrasting with impaired Figure Recall performance shown on the AMIPB⁹.

To summarize, performance on intelligence and memory measures revealed impaired information processing speed often seen after head injury. DD also showed impaired working memory, poor perceptual organization and performance-based IQ compared to verbal ability, impaired visual attention, impaired retention of complex verbal and visual material over time, impaired immediate retention of visual material, impaired ability to recognize visual stimuli amid distracters after a brief delay, impaired ability to match visual stimuli (faces) with corresponding verbal labels and intact ability to copy and remember simple visual shapes. Scores on the Hospital

Anxiety and Depression scale (HADS¹¹) reflected a mild degree of anxiety and depressive symptoms in the preceding week.

Imaging data

Images were obtained on a 3Tesla Philips Achieva scanner (Philips Medical Systems, Best, The Netherlands). The sequences obtained were; axial and coronal TSE T2 (TR 2067, TE 80); axial and coronal proton density (TR 2067, TE 17.78); T1 volume (TR 10.18, TE 4.691, flip angle 8, 0.8mm isotropic voxel size). The skull base demonstrated some congenital asymmetry with underdevelopment of the right petrous temporal bone. As a result of this there was some asymmetry to the shape of the overlying temporal lobes. Brain regions were otherwise normal. There was no evidence of any visible contusional damage to the lingual (medial occipitotemporal) gyrus or the fusiform (lateral occipitotemporal) gyrus on either side. Other areas commonly involved by contusional damage were also normal. Gradient echo and susceptibility weighted imaging are very sensitive to the presence of haemosiderin, a lasting product of intraparenchymal haemorrhage. There was no evidence of any haemosiderin staining in any region of the brain. The only abnormality was the presence of a small (8mm maximal diameter) colloid cyst at a typical location at the anterior end of the third ventricle. This was not obstructing the foramina of Monro and there was no lateral ventricular dilatation; however the cyst splayed the columns of the fornix.

[Insert figure 2 here]

[Insert figure 3 here]

DIFFERENTIAL DIAGNOSIS *If relevant*

TREATMENT *If relevant*

Therapy intervention approaches were designed as follows; rote rehearsal method required DD to study each randomly selected target letter by concentrating on the shape of the letter and any

distinctive figural features. The speech therapist presented the letter and enunciated the sound of the letter three times for approximately one second per letter to reinforce learning. DD completed both types of training within each session in counterbalanced order over ten sessions conducted over a three-week period. For the multimodal procedure DD was instructed to study the letter in detail and to think of an alternative stimulus beginning with the letter that he associated with the letter shape, for example 'm' reminded him of mountains because of up and down strokes, 's' reminded him of a snake because of its curved shape, and 'e' reminded him of an eye. This strategy created a phonemic link between the letter and the personal mnemonic prompt to enhance relevance and optimise learning. We also devised verbal descriptions of letter features, for example 'c' described as an incomplete circle with a section missing on the right hand side, 'l' described as a long vertical stick. The letters were reproduced in enlarged format. We asked DD to trace the shape of the letter while the therapist described visual features of the letter and reminded DD of the personal mnemonic prompt he had generated for the letter. On the third presentation DD was asked to generate a word beginning with the chosen letter (different from the mnemonic word generated earlier to aid recognition) to strengthen semantic word-letter associations. In this way multi-sensory (visual, auditory and tactile/kinetic) associations were made for each letter. We anticipated that this might prove more effective than the rote rehearsal method because that relies predominantly on visual/phonemic integration alone whilst the multimodal method synthesised multi-sensory information to enhance learning and depended upon mnemonic cues specifically generated by, and personal too, DD.

[Insert figure 4 here]

Figure four shows accuracy of ability to select target letters to a verbal prompt, and recognise and name target letters across ten therapy sessions in the rote rehearsal intervention. The letter 'i' was recognised as familiar and named correctly after one second following ten treatment sessions for the rote rehearsal method. Although four letters of this set (w, p, q and i) were considered to be familiar to DD, 'n', 'v' and 'w', and 'p' and 'q' were regularly confused. The average time to name each letter on session ten was 5 seconds, although only one response was accurate.

[Insert figure 5 here]

Figure five shows accuracy scores for letter selection familiarity and naming across ten sessions using the multimodal procedure. Plotted data show that the complete letter set was identified, named and rated as familiar by DD following the ten treatment sessions. Mean response time for letter naming was five seconds per letter, the same as for the rote rehearsal set, possibly indicating that although the multimodal letters had been learned identification was not automatic as with fluent reading. However, results of the initial intervention suggested that a multimodal approach to letter learning was more effective than rote learning in facilitating re-learning of letters and this approach was used for the 12 letters of the alphabet not yet studied in the second treatment block.

OUTCOME AND FOLLOW-UP

Results graphed in figure six show that the 12 remaining letters of the alphabet were remediated after ten additional therapeutic sessions using the multimodal intervention for letter relearning.

[Insert figure 6 here]

DISCUSSION *Include a very brief review of similar published cases*

Complete inability to recognize a single letter of the alphabet is rarely seen in alexia cases and when it does occur ability to write usually remains intact¹. Abstract representation of visual letters/words has been termed the ‘visual word form’¹²⁻¹³. The assumption is that recognition of the ‘word form’ enables fluent reading to occur across font, case, colour and size¹²⁻¹³. The term agraphia denotes individuals who have lost the capacity to write with reading ability generally intact; such cases are rare although more frequently documented than combined alexia and agraphia in the same individual as reported here¹⁴. Miozzo and Caramazza¹⁵ reported the case of GV, an 84 year-old woman who sustained a large left posterior brain lesion. GV was impaired at reading letters and numbers, and naming pictures, objects and colours. However, performance accuracy for naming tactile stimuli was at ceiling indicating intact access to non-visual word information. Agraphia indicates impaired writing when limb movements are intact¹⁴. This type of

impairment is associated with pathology affecting a region in left parietal cortex designated the Visual Word Form Area (VWFA), and thought to mediate letter recognition and letter imagery ability¹⁶⁻¹⁷.

The fornix is the major fibre tract connecting the hippocampal formation to basal forebrain and medial temporal regions associated with recall and episodic memory^{18, 20}. Cysts of the third ventricle abutting the fornix are often undetected until their presence causes increased intracranial pressure resulting in dilatation of ventricles and compacting of surrounding structures. Some authors report that ablation of the anterior column of the fornix does not induce memory dysfunction¹⁹. Others suggest that removal of a colloid cyst may cause anterograde amnesia and systematic disruption to episodic recall, although memory deficits are also seen prior to cyst removal^{2, 21}. Poreh et al¹⁸ reported impaired delayed visual recall on the Rey complex figure test (similar to the Figure Recall task used here) and severe visual and verbal memory deficits post-fornicectomy (see also Vann *et al*²²).

The current study presents the rare case of DD who exhibited global alexia and agraphia after a mild head injury. Structural imaging data revealed a third ventricular colloid cyst abutting the fornix sufficient to displace fornical columns. There was no additional pathology or ventricular dilatation. The presence of the cyst may be incidental to DD's clinical presentation but this seems unlikely; the slow emergence of functional deficits over several weeks post-injury suggests the unfolding of a pathological process. It is possible that the mild head injury was a catalyst for the development of the cyst but we have no way of confirming whether it was present *before* mild head injury²³. Neuropsychological testing revealed general widespread memory deficits across visual and verbal domains (worse for visual stimuli) that disproportionately impeded reading and writing ability, slowed processing speed, and impoverished Story and (complex) Figure Recall. Arguably, DD's visual memory problems took the form of a general visual imaging and visual processing deficit that abolished visual invariance (i.e. the stable capacity to recognize letters across different fonts and viewpoints etc). Several researchers have theorized that clinical features of alexia and agraphia are subtended by visual imaging deficits or a general visual processing

deficit although the mechanism is thought to be different for each condition^{12, 14-16}. We are not aware of any theory proposing that the same structural impairment might drive both conditions post-neuropathology possible reflecting few reported cases of complete alexia and agraphia in the same individual. DD reported that presently, several years after the accident he is only able to cursively write (typing is relatively fluent) by imaging letters that he was trained on. He claims that he is unable to vary the visual representation of the training letter by changing the font, colour or size of the image. DD was able to draw a generic house on command possibly by utilizing a verbal description of a house, but was unable to draw *his* house. He appeared to have lost the capacity to ‘free image’ letters and likely other stimuli (his house) indicated by neuropsychological test results, that required a type of visual ‘fluency’.

To conclude, the distinction between alexia and aphasia at functional and structural levels might be broadly considered an artefact of the conceptualization of these disorders. Alexia and agraphia cases are seldom reported in a manner that evaluates the potential for shared functional deficits affecting reading and writing. On functional tests, DD showed general memory impairments that predominantly affected visual recognition memory and imaging ability adversely affecting. Our case suggests that there might be some global visual mechanism shared across alexia and agraphia that at present we can only conceptualize as ‘free’ visual imaging whereby a representation is self-generated rather than exactly reproduced from a previously seen item and that accounts for perceptual invariance in visual recall. Findings raise questions about the purported neural substrates of reading and writing, the general role of fornical connectivity to memory, the importance of visual recognition memory and visual imaging to reading and writing, and the efficacy of multimodal methods in reading retraining.

LEARNING POINTS/TAKE HOME MESSAGES 3 to 5 bullet points – this is a required field

- Displacement of fornical tract connectivity can induce visually mediated functional deficits.
- Gross grey matter lesions are not necessary for reading and writing deficits to be present

after head injury.

- Fluent reading and cursive writing ability may depend on a type of visual ‘fluency’ for abstract letter manipulation.
- Multi-modal rather than rote rehearsal training can remediate profound reading and writing deficits.

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Table 1: DD’s scores on neuropsychological tests of intelligence, attention and memory

Function tested	Score: Percentile
Intelligence (WAIS III³⁰)	
Full Scale IQ	107 (68%)
Verbal IQ	110 (75%)
Performance IQ	99 (47%)
Verbal Comprehension Index	120 (91%)
Perceptual Organisation Index	109 (73%)
Working Memory Index	95 (37%)
Processing Speed Index	73 (4%)
Visuospatial perception (VOSP³¹)	
Screening Test	19/20
Silhouettes	26/30
Dot Counting	10/10
Position Discrimination	20/20
Number Location	9/10
Cube Analysis	10/10
Visual and auditory attention (TEA³²)	
Map Search:	
Symbols circled - one minute:	27 (1-5 th %)
Symbols circled - two minutes:	45 (10-25 th %)
Elevator counting:	7 (100%)
Elevator counting with distraction:	10 (75 th %)
Attention Memory and Information Processing Battery (AMIPB³³)	
Verbal list learning Total A1-A5:	55 (25 th %)
Distractor list:	6 (50 th %)
Target list after distractor:	12 (25-50 th %)
Story Recall Immediate:	31 (10-25 th %)
Delayed:	17 (2.5-10 th %)
Retained:	55% (< 2.5 th %)
Figure Recall Copy:	80 (75 th %)
Immediate:	42 (< 2.5 th %)
Delayed:	28 (< 2.5 th %)
Retained:	66% (< 2.5 th %)
Visual/Verbal recall and recognition (Doors and People³⁴)	
Doors:	18 (5 th %)
Shapes:	13 (1-5 th %)
Verbal forgetting scores	36 (> 90 th)
Visual forgetting score	2 (25 th)
	1 (50%)

* Raw scores provided for all subtests

FIGURE/VIDEO CAPTIONS *figures should NOT be embedded in this document*

Figure 1. Figure recall from AMIPB: copy with picture present, immediate and delayed copies without picture.

Figure 2: MRi showing location of colloid cyst in third ventricle in coronal, sagittal and axial planes.

Figure 3: Intact left Visual Word Form Area region of interest in coronal, sagittal and axial planes; Imaging data show intact mid fusiform gyrus on the left with region of interest identified by crosshairs.

Figure 4: Results of rote rehearsal letter remediation intervention, familiarity, selection and letter naming scores. Target letters: n, p, v, q, i, w.

Figure 5. Results of multimodal letter remediation intervention, familiarity, selection, and letter naming scores after ten sessions. Target letters: g, r, s, l, h, b.

Figure 6: Results of multimodal letter remediation intervention for remaining untreated 12 letters

of alphabet, familiarity, selection and letter naming scores after ten sessions. Target letters: z, j, e, y, a, k, u, c, f, m, t, d.

PATIENT’S PERSPECTIVE *Optional*

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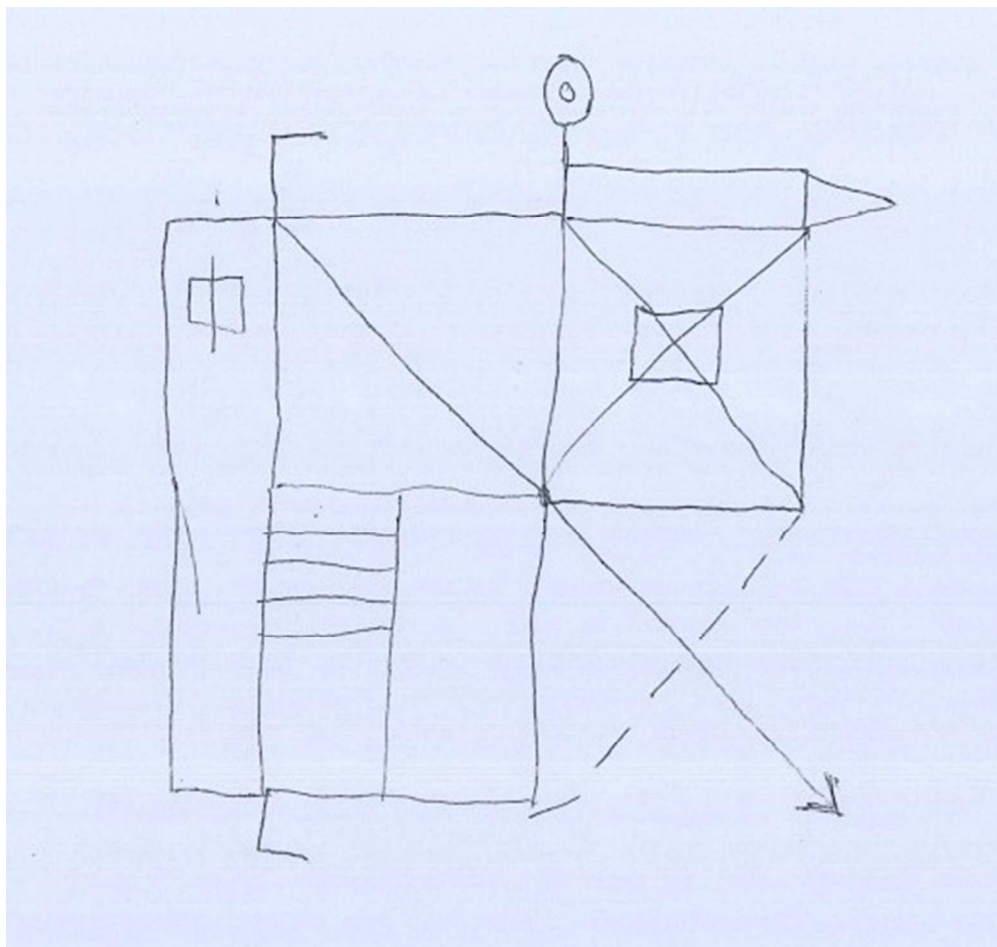
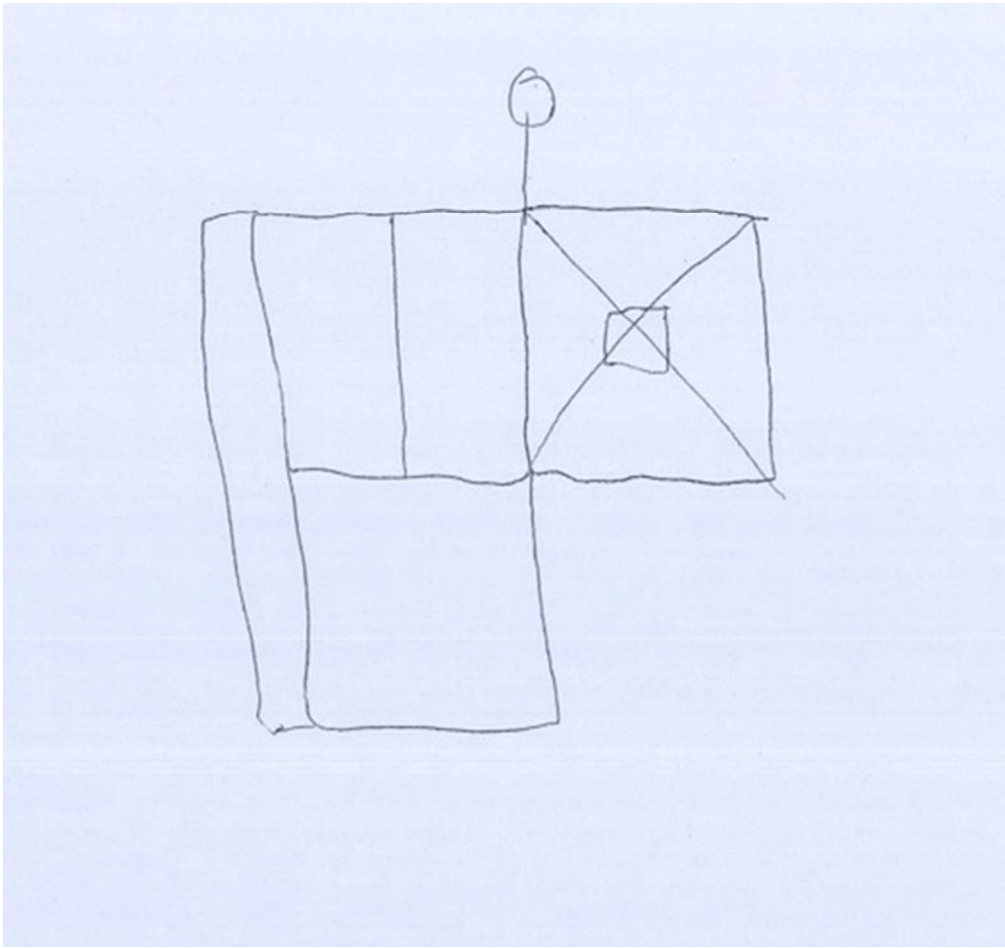
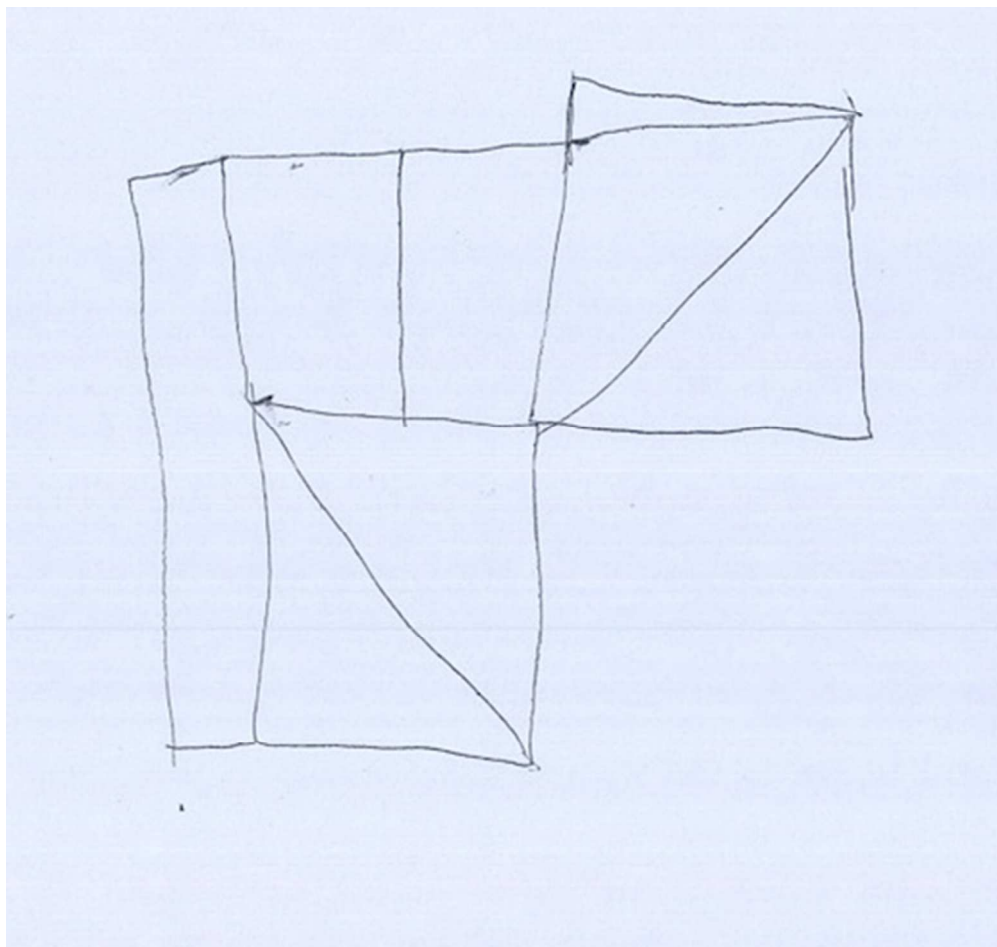


Figure 1a, b, c, recall from AMIPB: copy with picture present, immediate and delayed copies without picture.
137x129mm (96 x 96 DPI)



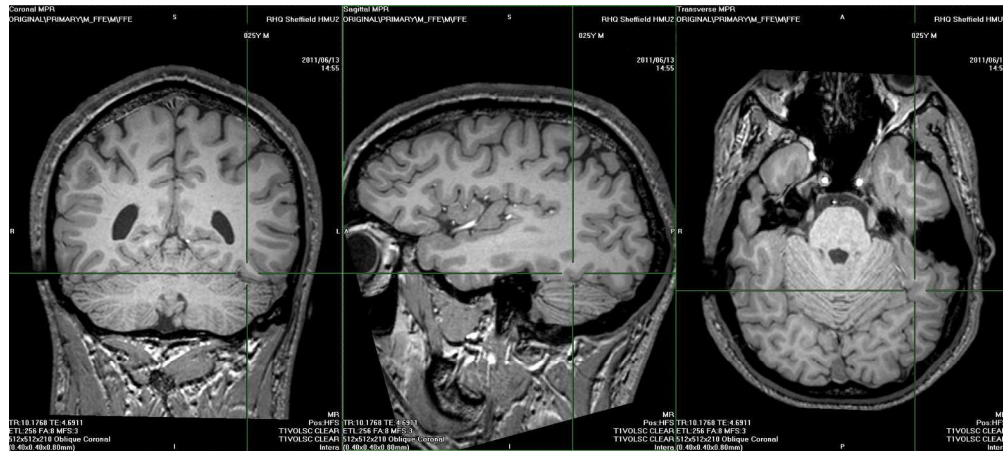
Immediate copy
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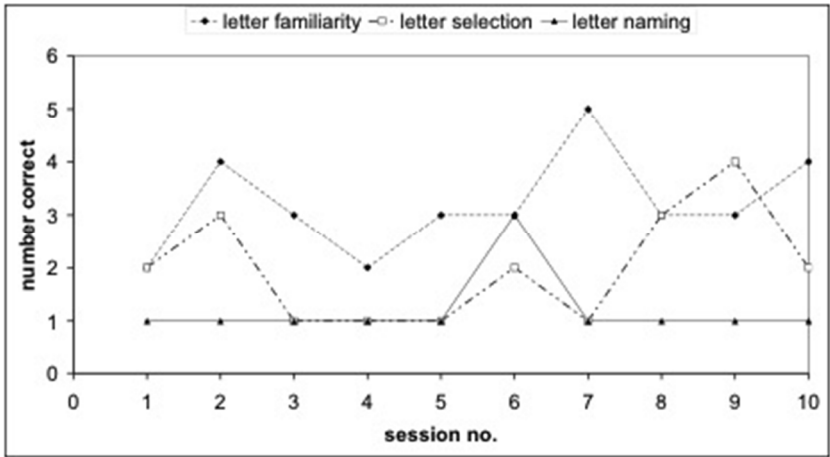
Delayed copy
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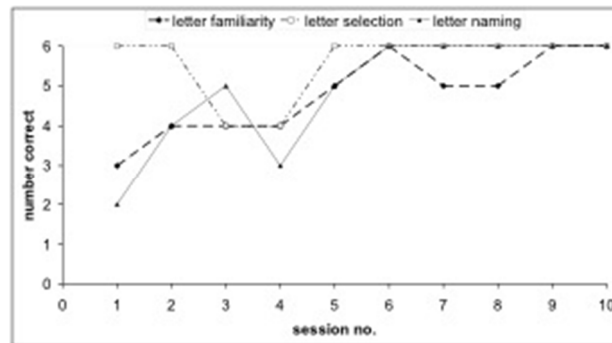
MRI showing location of colloid cyst in third ventricle in coronal, sagittal and axial planes.
524x233mm (96 x 96 DPI)



Intact left Visual Word Form Area region of interest in coronal, sagittal and axial planes; Imaging data show intact mid fusiform gyrus on the left with region of interest identified by crosshairs.
524x233mm (96 x 96 DPI)



Results of rote rehearsal letter remediation intervention, familiarity, selection and letter naming scores.
Target letters: n, p, v, q, i, w.
146x80mm (72 x 72 DPI)



Results of multimodal letter remediation intervention, familiarity, selection, and letter naming scores after ten sessions. Target letters: g, r, s, l, h, b.
108x60mm (72 x 72 DPI)

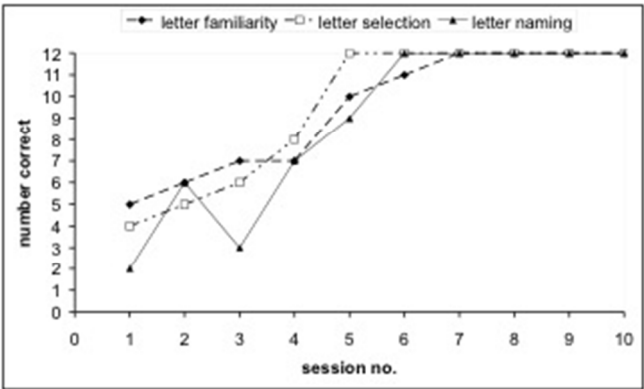


Figure 6: Results of multimodal letter remediation intervention for remaining untreated 12 letters of alphabet, familiarity, selection and letter naming scores after ten sessions. Target letters: z, j, e, y, a, k, u, c, f, m, t, d.
114x69mm (72 x 72 DPI)