

# Neuroimaging Findings in a Patient Recovering from Global Alexia to Spelling Dyslexia

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## ABSTRACT

The authors report findings in a 67-year-old right-handed man who had an ischemic infarct in the territory of the left posterior cerebral artery. The clinical manifestation consisted mainly of total alexia without agraphia. The patient gradually recovered, subsequently showing the syndrome of spelling dyslexia. Cerebral MR-images revealed a circumscribed infarction of medial and basal parts of left temporal lobe. In the acute stage [ $^{99m}\text{Tc}$ ]HM-PAO SPECT was characterized by a diminished uptake in the definitely infarcted area and hyperfixation in the region of the left forceps major. Because high retention of HM-PAO indicates potentially salvageable tissue after an ischemic event, the depicted area might be correlated with the recovery of function. Thus, the authors' neuroimaging data give further support to the assumption that the left forceps major is a critical area for global alexia, whereas spelling dyslexia is due to involvement of the left medio-basal temporal lobe.

Key words: global alexia, spelling dyslexia, recovery of function, [ $^{99m}\text{Tc}$ ]HM-PAO SPECT, HM-PAO hyperfixation, magnetic resonance imaging.

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Global alexia without agraphia is a rare manifestation of occipital ischemic infarction, first described by the French neurologist Déjerine in 1893.<sup>1</sup> Since that time, further cases have been added analysing the underlying conditions in order to elucidate the pathogenesis of the syndrome.<sup>2</sup> We report a new case and neuroimaging data.

## Patient Report

A 67-year-old right-handed man had an ischemic infarct in the area supplied by the left posterior cerebral artery after

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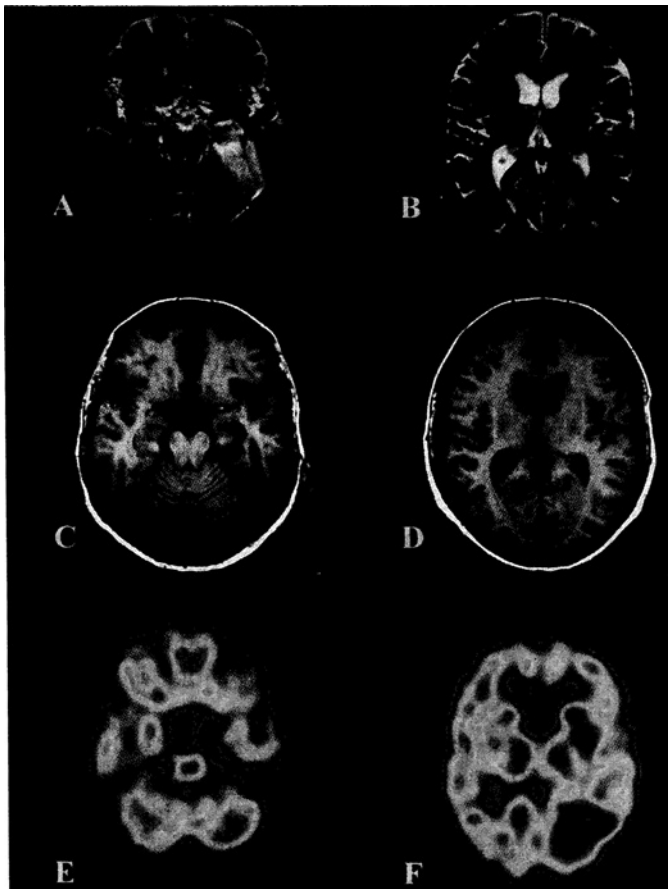
transient premonitory symptoms such as incapacity to read aloud, vertigo, nausea, and vomiting. Hours later he realized that he had lost the capability to read.

After admission the patient presented with global alexia without agraphia. Although he was able to write subtly about a complex issue, he was unable to read what he had written. The written text was correct regarding grammar and content, but there were a few phonetic errors. Apart from slight anomia, speech was fluent and comprehension intact. Additional symptoms were a superior quadrantanopsia to the right and minimal ataxia of the trunk. In general, the patient complained of amnesic difficulties.

Magnetic resonance imaging (MRI) was performed on day 2 of the affection and additionally, a single-photon emission computed tomography (SPECT), using [ $^{99m}\text{Tc}$ ]HM-PAO (hexamethyl propylene amine oxime), on day 8. Cerebral T1- and T2-weighted MR-images showed a circumscribed cerebral infarction of the left medio-basal part of the temporal lobe (Fig 1A, C) extending to the occipital horn of the lateral ventricle. No definite infarction was disclosed in the adjacent occipital white matter, there was only minor ischemic signal alteration in the acute phase (Fig 1B, D). The [ $^{99m}\text{Tc}$ ]HM-PAO SPECT study showed a mixed pattern: in the medio-basal part of the left temporal lobe, where definite infarction had occurred, HM-PAO-uptake was diminished (Fig 1E); and, in a circumscribed zone of the left occipital white matter involving the forceps major, a marked HM-PAO hyperfixation was found, compatible with hyperperfusion after early reperfusion (Fig 1F).<sup>3,4</sup> These areas correspond to subterritories of the lateral branch of the posterior cerebral artery (see discussion), whereas the calcarine area and the parieto-occipital cortex, supplied by the medial branch, were not affected in any of the two examination modalities.<sup>5</sup>

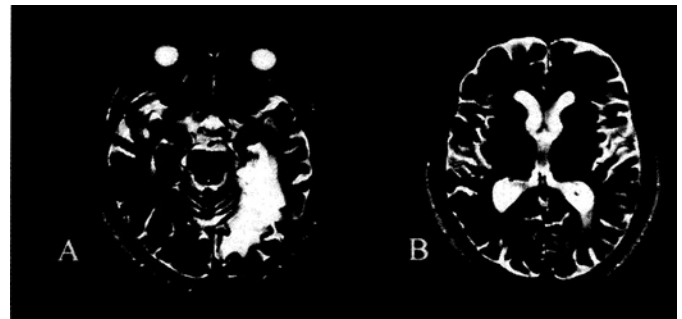
The patient gradually recovered over the next 3 months showing two major reading strategies, i.e., a laborious letter-by-letter method<sup>2</sup> and later the so-called "whole-word procedure"<sup>6</sup>: reading his hand-writing he first spelled the letters and then put them together to form a word, sometimes misreading the beginning or the end of the word. Later he tried to remember a word by associating the occasion on which he wrote it. Finally, he was able to recognize words faster than before, as he remembered more and more the symbols representing a whole word. Initially this was possible for short nouns only, later also for longer words of any type.

Conditions did not change in the course of three years. The compensatory strategies became more routine allowing more or less fluent, albeit slow reading. When fatigued the patient sometimes confused letters such as "b," "p," and "d." *Neuropsychological testing*, at this stage, gave evidence for intact visual object and visual space percep-



**Fig 1.** Synopsis of correlated T2- (A, B) and T1-weighted (C, D) MRIs, and [<sup>99m</sup>Tc]HM-PAO brain SPECT slices (E, F) from days 2 and 8, respectively. In the left column definite infarction is demonstrated in the medio-basal part of the left temporal lobe by MR-images (A, C), concordant with low HM-PAO uptake by SPECT (E). The right column (B, D, F) shows the findings at the level of the posterolateral white matter. Prominent findings are hyperfixation of HM-PAO by SPECT involving the forceps major, whereas in the corresponding MR-images subtle ischemic changes are seen in the occipital white matter. Image plan is parallel to the line between anterior and posterior commissure. (For methodical questions see reference 8). View is from below, so that the right hemisphere appears on the left.

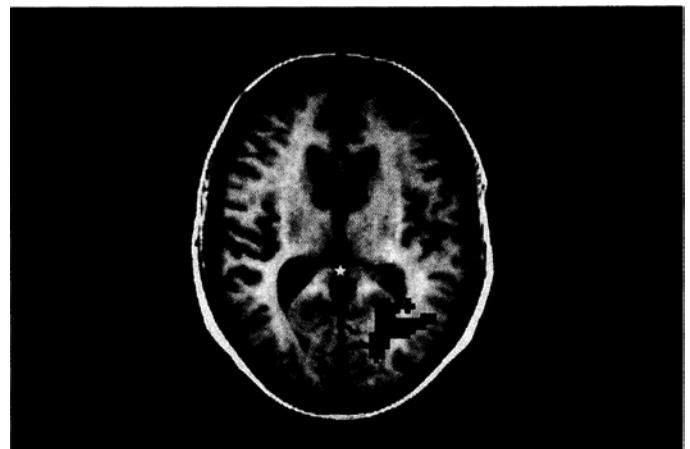
tion (VOSP). Visual-constructive abilities (Rey-Osterrieth Complex Figure Test) were normal as well as figural learning and memory as evinced by the Rey Visual Design Learning Test (RVDLT). There was no apraxia. Aachen Aphasia Test and Basel-Minnesota Test showed normal findings except for a few phonetic errors when reading aloud ( $\approx 5\%$ ). This errors concerned preferentially abstract words and nonwords. Hand-writing was perfectly preserved. Processing of numerals was intact. Learning and memory for written (CERAD, Consortium to Establish a Registry for Alzheimer's Disease) and listened word lists (CVLT, California Verbal Learning Test) were significantly impaired. In the Chapman-Cook Reading Test, reading aloud was slowed and time consumed for comprehension of a text was significantly prolonged. Reading his



**Fig 2.** Follow-up examination showing T2-weighted MR-images (A, B) at levels comparable to Fig 1, 3 years later. Because the examination was not coregistered with the first image plan is slightly anteflected in comparison to Figure 1. Encephalomalacic area in the left medio-basal temporal lobe (A) and gliosis in the occipital white matter (B).

own written text was considerably slowed over reading a printout of the same text (75 words/min vs. 106 words/min). The ability to read and write shorthand was definitely lost. Summarizing, the observed behavioral pattern suggested severe difficulties both for learning and recalling of verbal material. Obviously, difficulties of reading increased in parallel to formal reductions of characters used, from printed material to hand-written texts and, finally, to texts in shorthand.

Follow-up MRI did not reveal new aspects (Figs 2A, B). Postischemic encephalomalacia had occurred in the left medio-basal temporal lobe, whereas only a slight gliomatous alteration was detected in the occipital white matter sparing the forceps major.



**Fig 3.** Parametric map of [<sup>99m</sup>Tc]HM-PAO brain SPECT, indicating a cluster of deviating pixels with a z-score of  $>+2.5$ , after integration into the appropriate anatomical MR-image. The brain studies were spatially standardized according to the reference brain of CBA. The symbol (\*) indicates the lower part of the splenium corporis callosi. Note partial confirmation of the qualitative assessment (see Fig 1F) by the quantitative analysis, showing significantly enhanced HM-PAO up-take in the left postero-lateral white matter including forceps major. According to Talairach and Tournoux,<sup>14</sup> the center of deviating pixels has the coordinates  $x = -24$ ,  $y = -66$ ,  $z = 8$ .

## Image Analysis

For quantitative analysis and localization, SPECT data were merged into a dedicated Computerized Brain Atlas (CBA) system.<sup>7</sup> The system makes it possible to reorientate and standardize image data and, thus, to merge functional data with anatomical details of MR-images.<sup>8</sup> With regard to SPECT data z-scores were calculated on a pixel basis for each slice in comparison to a population of 24 normal volunteers (age range 25 to 63 years). By thresholding parametric images were obtained, indicating deviating pixels: by this analysis the zone of HM-PAO hyperfixation could be located outside the definitely infarcted area. According to the z-statistics performed, HM-PAO hyperfixation was confined to the adjacent white matter of the temporo-occipital junction. It corresponded to a large cluster of pixels, with a z-score of more than +2.5, which is demonstrated in Figure 3 after integration into the corresponding MRI slice.<sup>8</sup>

## Discussion

Pure alexia without agraphia was first reported by Déjerine in 1893,<sup>1</sup> defined as a syndrome characterized by the inability to read aloud or to comprehend words in the absence of aphasia. The traditional account attributes the syndrome to a disconnection between circumscribed areas of the left and right hemisphere.<sup>2</sup> Thus, lexical and semantic analysis of the right hemisphere is not accessible to the language processors on the left.<sup>6</sup> While a few similarly affected cases have been described by others, it is clear that most patients with left posterior hemisphere injury do not present with a uniform manifestation of global alexia.<sup>6,9-12</sup> Binder and Mohr<sup>2</sup> differentiated between global alexics and spelling dyslexics. The latter describes exactly the stage of recovery in our patient. Characteristically he used the residual capacities to overcome his deficit: first, he predominantly applied the letter-by-letter method, and later on the so-called "whole-word procedure" as described above.<sup>6</sup> Correlating reading deficits with lesion topography typical lesion sites within the left posterior cerebral artery territory were described: (1) normal readers had lesions in the medial and ventral occipital lobe, sparing dorsal white matter and the medial-ventral temporal lobe; (2) global and permanent alexia occurred only when the splenium of the corpus callosum, forceps major or the white matter above the occipital horn of the lateral ventricle were injured. (3) patients with "spelling dyslexia" had lesions of the medial and ventral temporal lobe.<sup>2</sup>

While our patient presented with global alexia, a mixed perfusion pattern was present in the [<sup>99m</sup>Tc]HM-PAO SPECT study, affecting the vascular territory of the lateral branch of the posterior cerebral artery.<sup>5</sup> According to Salomon and Huang,<sup>13</sup> this territory is subdivided into subterritories supplied by an inferior temporal and an occipitotemporal artery. The two distinct perfusion patterns

indicated quite different prognosis for the affected brain tissue: at the site of low HM-PAO uptake, at the left medio-basal temporal lobe, ischemic infarction was evident even by MR-imaging in the acute stage. In contrast, the zone of HM-PAO hyperfixation, in the white matter of the occipito-temporal junction, recovered almost completely as verified by follow-up MR-imaging. We suggest that recovery is due to early reperfusion as observed in recent SPECT studies. However, since SPECT was performed at a later stage of subacute infarction, reparative mechanisms, i.e., granulomatous tissue, might have accounted additionally for enhanced HM-PAO uptake in the ischemic area.<sup>3</sup> In conclusion, HM-PAO hyperfixation during the acute stage of stroke might represent an index of endogenous neuroprotection by reduced oxidative stress and, thus, indicate a favorable prognosis.<sup>3,4</sup> Our observation is in accordance with the basis of the theory that the splenium of the corpus callosum and the left forceps major are critically involved in global alexia, and that a lesion of the left medial and ventral temporal lobe is associated with spelling dyslexia.<sup>2</sup>

In conclusion, the mixed pattern of HM-PAO retention in the SPECT study provided the opportunity to understand the partial recovery from global alexia. It showed a differential affection of the susceptible areas, in which HM-PAO hyperfixation delineated the potentially reversible part of the syndrome. With regard to Figure 3, we suggest a temporary deafferentiation of the left occipitoparietal association cortices.

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