Supplementary Methods

Method 1: Exclusion criteria

The main exclusion criteria were as follows: (1) known conditions (other than stroke) affecting cognition including neurological conditions (mental retardation, Alzheimer's disease or related condition, epilepsy, severe traumatic brain injury, Parkinson's disease, multiple sclerosis, a brain tumor, or brain radiotherapy), (2) previously diagnosed psychiatric conditions (schizophrenia and major psychiatric disorders requiring hospitalization for >2 days in a specialized setting), (3) general comorbidities (chronic alcoholism, substance addiction, liver, kidney, or respiratory failure, and paraneoplastic syndrome), (4) treatments affecting cognition (other than stable dosage levels of an anxiolytic or a serotoninergic antidepressant), (5) conditions precluding cognitive assessment (illiteracy, severe sensory or motor impairments, or alertness disorder—defined as a score ≥1 for item 1a of National Institutes of Health Stroke Scale [NIHSS]), (6) co-morbidities associated with a life expectancy <2 years, (7) contra-indication to magnetic resonance imaging (MRI), (8) large cerebellar lesions (as they precluded the determination of uptake value), (9) pregnancy, (10) legal guardianship, and (11) lack of written informed consent. The presence of aphasia, hemineglect, prior stroke, and abnormal Informant Questionnaire on Cognitive Decline in the Elderly (defined as score ≥55 for the 16 items version) were not exclusion criteria provided it was not due to a diagnosed disease other than stroke (such as Alzheimer's disease). As previously indicated,[13] patients unable to perform a cognitive test due to cognitive impairment (including aphasia) were considered impaired.

Method 2: Cognitive score combination

According to a previously validated procedure,[14] component scores were combined according to the cognitive domain: when several component z scores assessed the same domain, they were averaged to yield a domain score (action speed: Trail Making Test part B and digit symbol substitution test; cognitive executive functions: semantic fluency, "PVR" fluency, error on Trail Making Test part B minus error on Trail Making Test part A; episodic memory: third and delayed free recall of Free Cued Selective Reminding test; language: Shortened Boston Naming test; and visuoconstructive abilities: copy of the Rey–Osterrieth complex figure test). After checking the homogeneity of the score distribution across the domains, the five domain scores were combined in the overall cognitive summary score, corresponding to the average of the five domain scores. Finally, the scores were categorized (i.e., normal or impaired) using the 5th percentile. Missing data were only interpreted as corresponding to an impairment when the neuropsychologist indicated that the patient was unable to perform the task.

Method 3: Amyloid positron emission tomography

Quantitative analyses were also performed according to the recommended methods.[15] Volumes of interest (VOIs) were applied to individual MR images and transferred to the co-registered positron emission tomography (PET) images using PMOD V3.407 (PMOD Technologies Ltd., Zurich, Switzerland). A composite VOI including frontal, parietal, lateral temporal and occipital cortex as well as the posterior cingulate was created, and the corresponding standardized uptake value ratios (SUVr) were calculated with the cerebellar cortex as a reference.[15] To avoid a confounding influence by the stroke lesion, the lesion mask (delineated on the corresponding MRI according to a previously validated method[15]) was excluded from the composite VOI on the PET data.

Patients with a global florbetapir SUVr ≥1.35 were considered to be amyloid positive. There was perfect agreement between the visual and quantitative interpretations (κ=1, P=0.0001).

To examine whether stroke lesion could have promoted amyloid deposition, two additional analyses were performed. First the SUVr of the peri-stroke region were determined in the 70 first patients (negative results led to the discontinuation of this analysis) and they were compared to those of the homologous region in the contralateral hemisphere using the methods of Wollenweber.[10] Briefly, the peri-stroke VOIs were drawn manually around the stroke lesion (using lesion mask delineated according to a previously validated method). The peristroke VOIs were then flipped on the y axis to determine the VOI in the homologous region of the contralateral hemisphere. SUVr was then calculated in both peri-stroke and homologous VOIs. They were compared using paired t-test. Second, we separately calculated the composite VOI of the ipsilesional and contralesional hemispheres. Their relationship was assessed using a correlation analysis between the composite VOIs of the ipsilesional and contralesional hemispheres.