# POST STROKE DEMENTIA: DIAGNOSIS & INTERVENTION

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**Barrow Neurological Institute Stroke Symposium**

**October 13, 2018**

BARROW Neurological Institute

Dignity Health™ St. Joseph's Hospital and Medical Center

# Overview

- Stroke & Cognitive Impairment
  - The VCI continuum & terminology
- The presentation & diagnosis of PSD
  - Where & how much?
  - Complications of diagnosis
- Neuropsychological evaluation of PSD
  - Cognition, Mood, & Functional ability
- Intervention
  - Before & after stroke
  - Future directions: DMTs

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# Stroke is a leading cause of disability

- Among adults age 45–69 years, heart disease and stroke are the leading causes of death and lost disability-adjusted life years (DALYs) worldwide (Strong et al., *Lancet Neurol,* 2007*)*

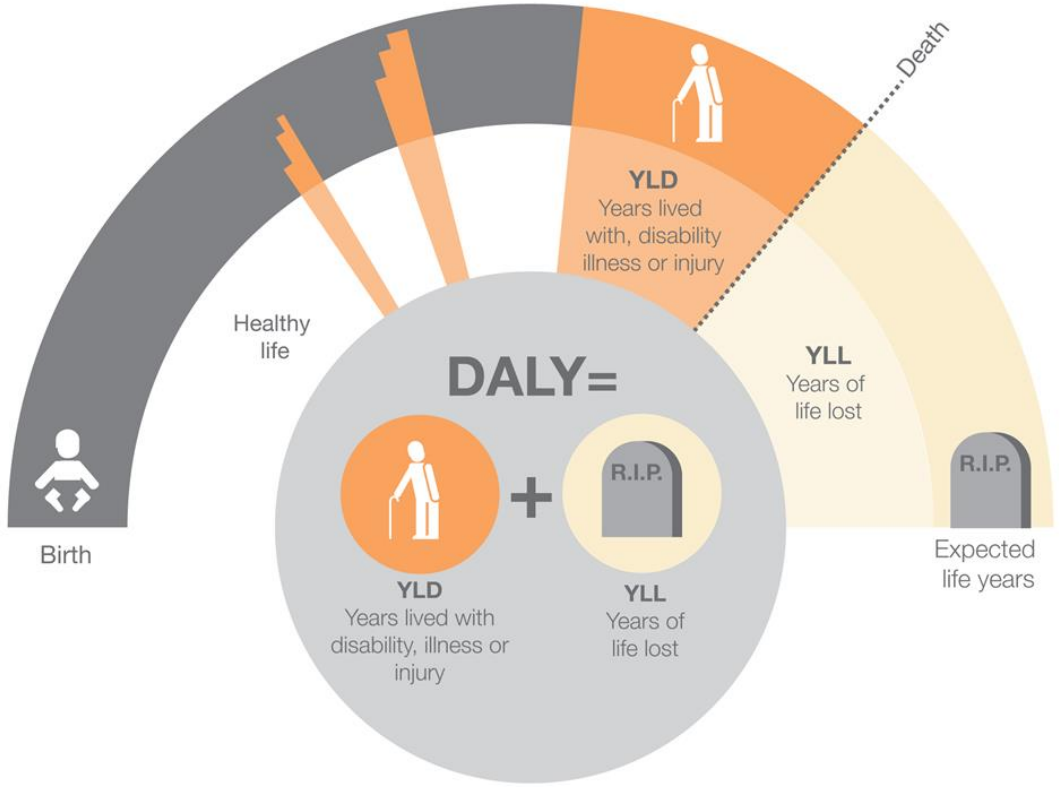


Image from Public Health England

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# Types of Stroke

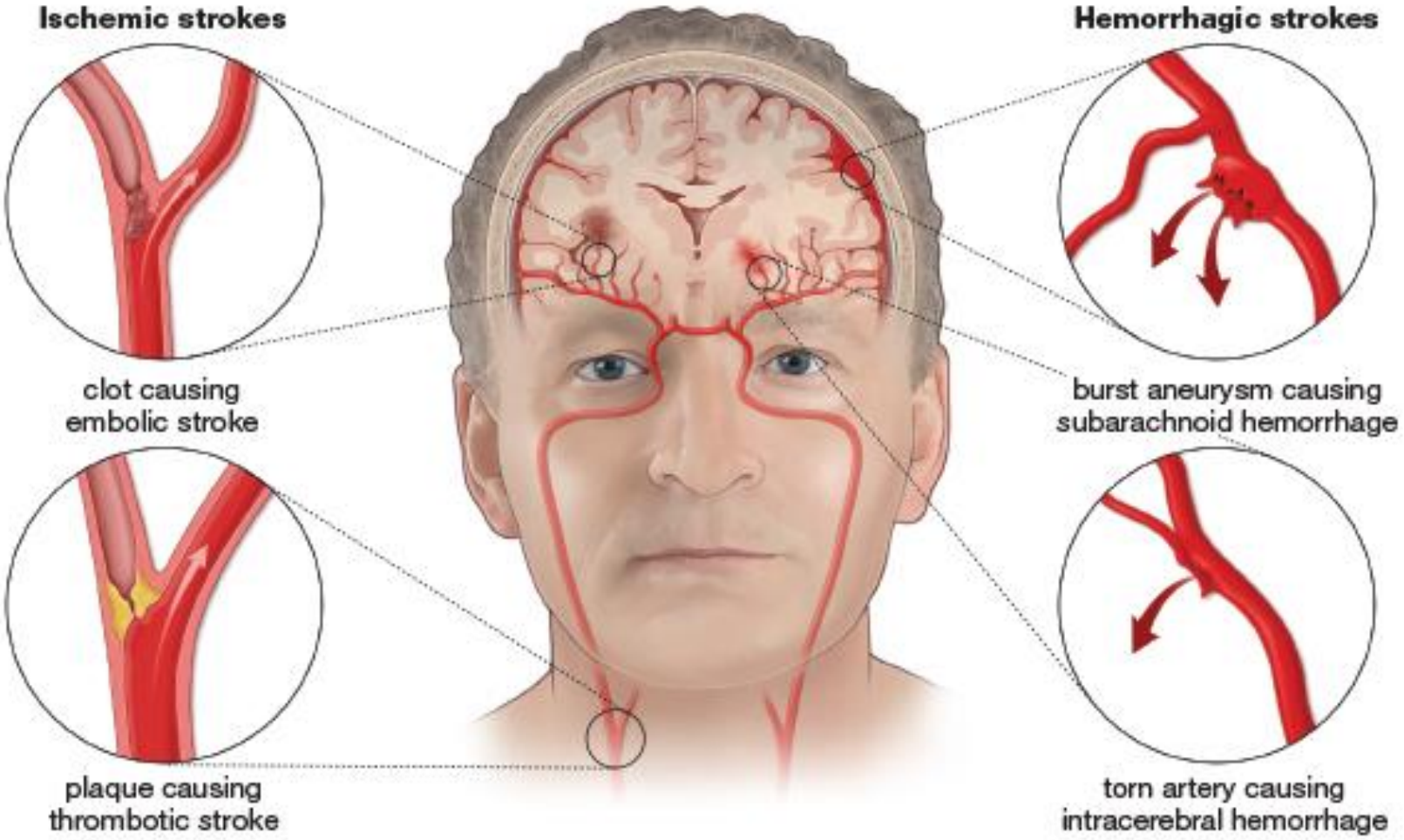


Image from HealthCentral.com

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# Why cognitive impairment after stroke matters

- Research has historically focused on physical disability following stroke, but cognitive impairment affects daily functioning, quality of life, and return to work to an equal degree
- Stroke survivors are at risk for cognitive impairment due to overlapping factors
  - Acute tissue damage
  - Cognitive decline associated with age
  - Comorbid vascular risk factors
  - Pre-existing subclinical vulnerability (e.g. amyloidopathy)
- Physical impairments often improve to some degree after stroke; however cognitive impairments often progressively worsen

Mijajlović et al. *BMC Medicine* (2017)

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# Stroke Survival

- Risk factors for stroke are increasingly prevalent
  - Hypertension
  - Atherosclerosis
  - Hyperlipidemia
  - Type II diabetes
  - Obesity

- Meanwhile, death from stroke is decreasing
  - 40.6 per 100,000 in 2008
  - You are 75% less likely to die of stroke now compared to 1950 (Towfighi et al. 2011).

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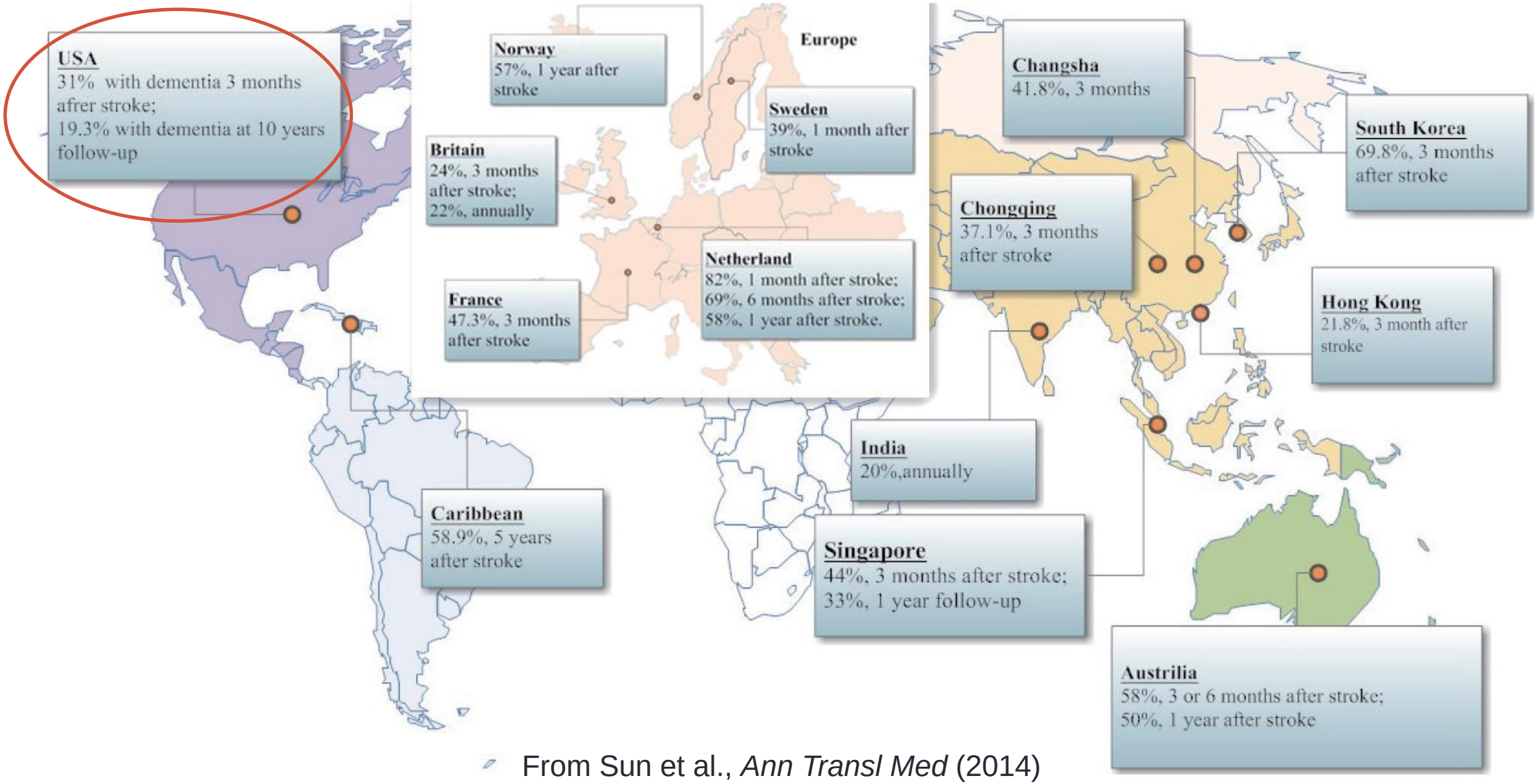
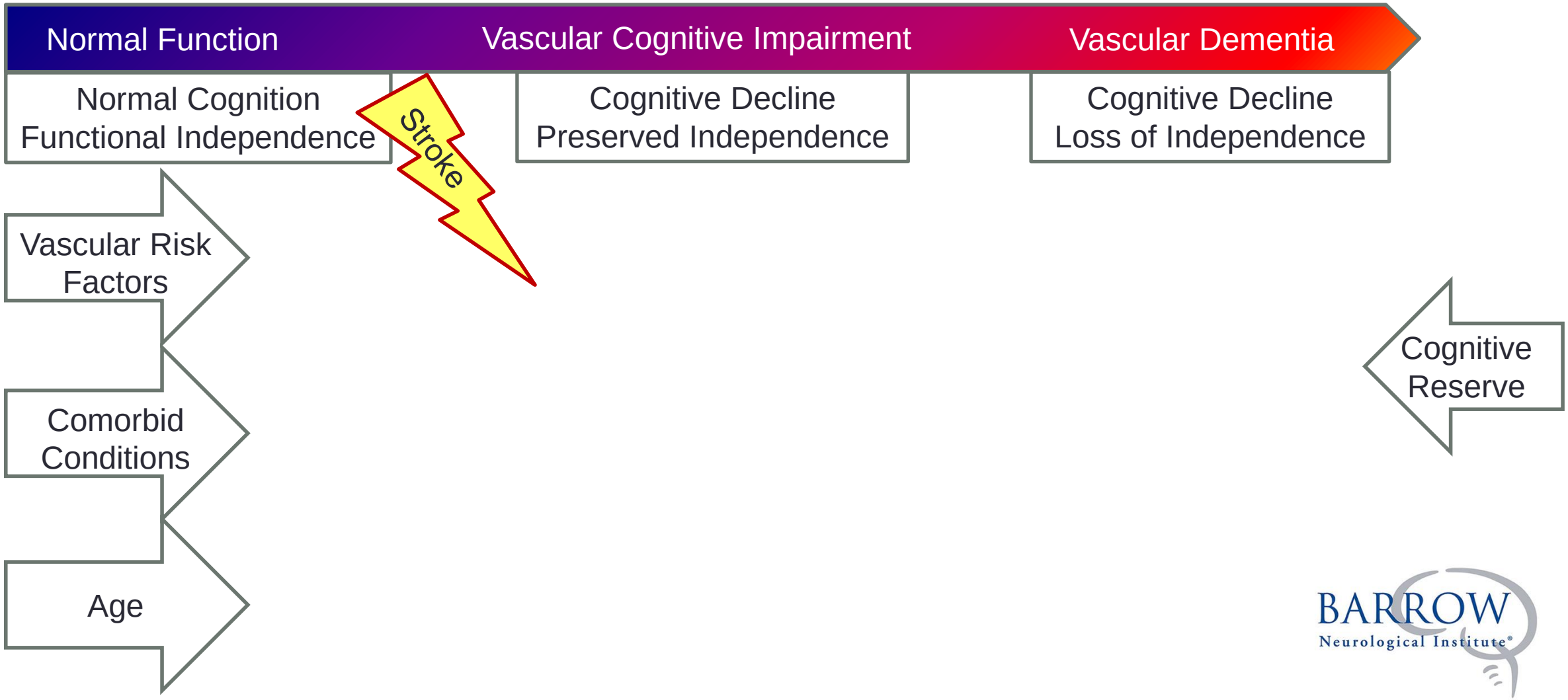



- From Sun et al., *Ann Transl Med* (2014)

# Stroke, Vascular Cognitive Impairment, & Dementia

- PSCI/PSD is diagnosed when cognitive impairment first emerges after a stroke
- This is often difficult to ascertain since VCI/VaD may be present but unrecognized prior to stroke
- Stroke, especially ischemic stroke, often occurs along a continuum of VCI and includes risk factors which may be pre-existing

# The VCI continuum & stroke

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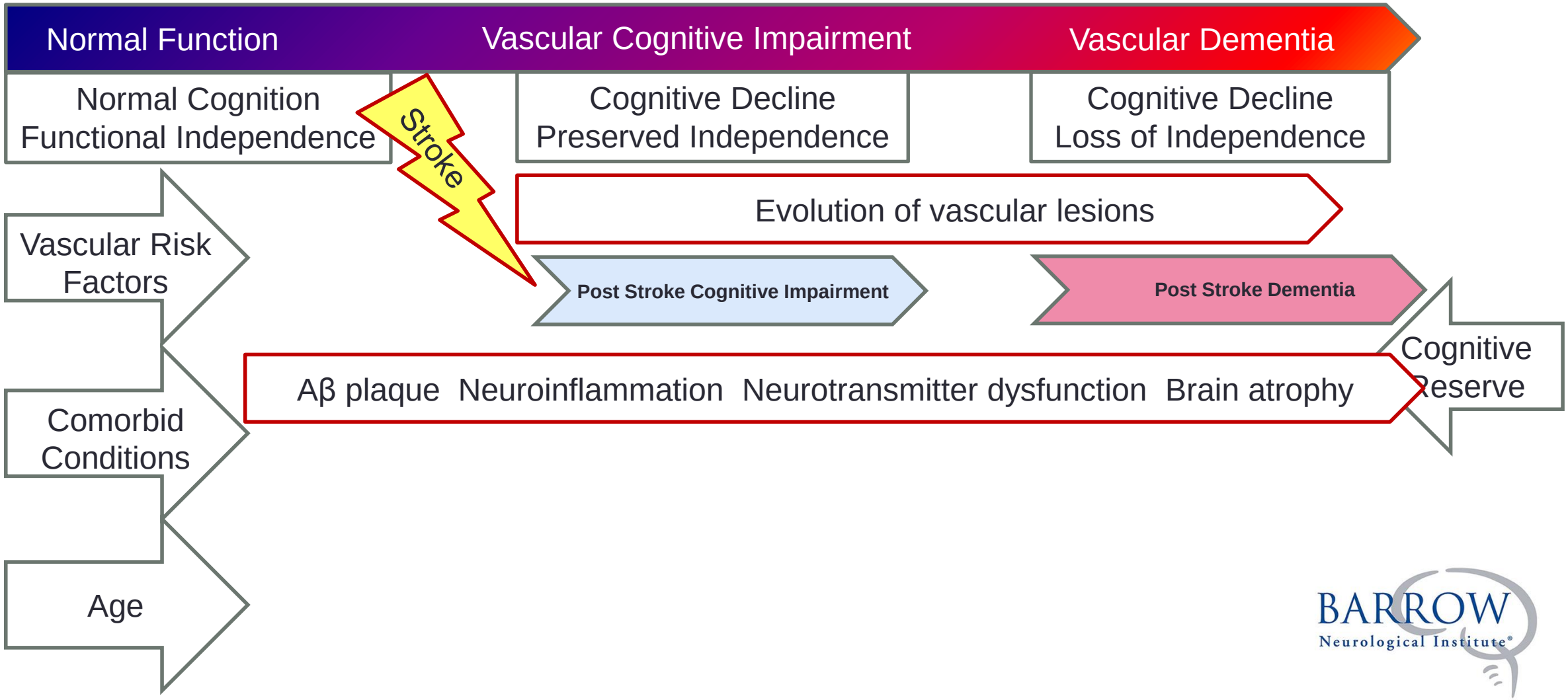
# Complications of diagnosis

- Established diagnostic criteria for dementia may not be suitable to stroke populations
- As in other forms of dementia, PSD vs. PSCI is based on limitations in ADLs; however, physical impairments following stroke may impede assessment of changes in ADLs specifically related to cognitive problems
- Definitions of dementia emphasize multi-domain cognitive impairment and memory deficits; however, in stroke, it is possible to have disabling cognitive problems but retain memory
- Stroke patients are typically older and may have (diagnosed or undiagnosed) pre-stroke cognitive decline, precluding a diagnosis of PSD
- Moreover, tissue damage continues to evolve after stroke

# Post Stroke Cognitive Impairment & Dementia

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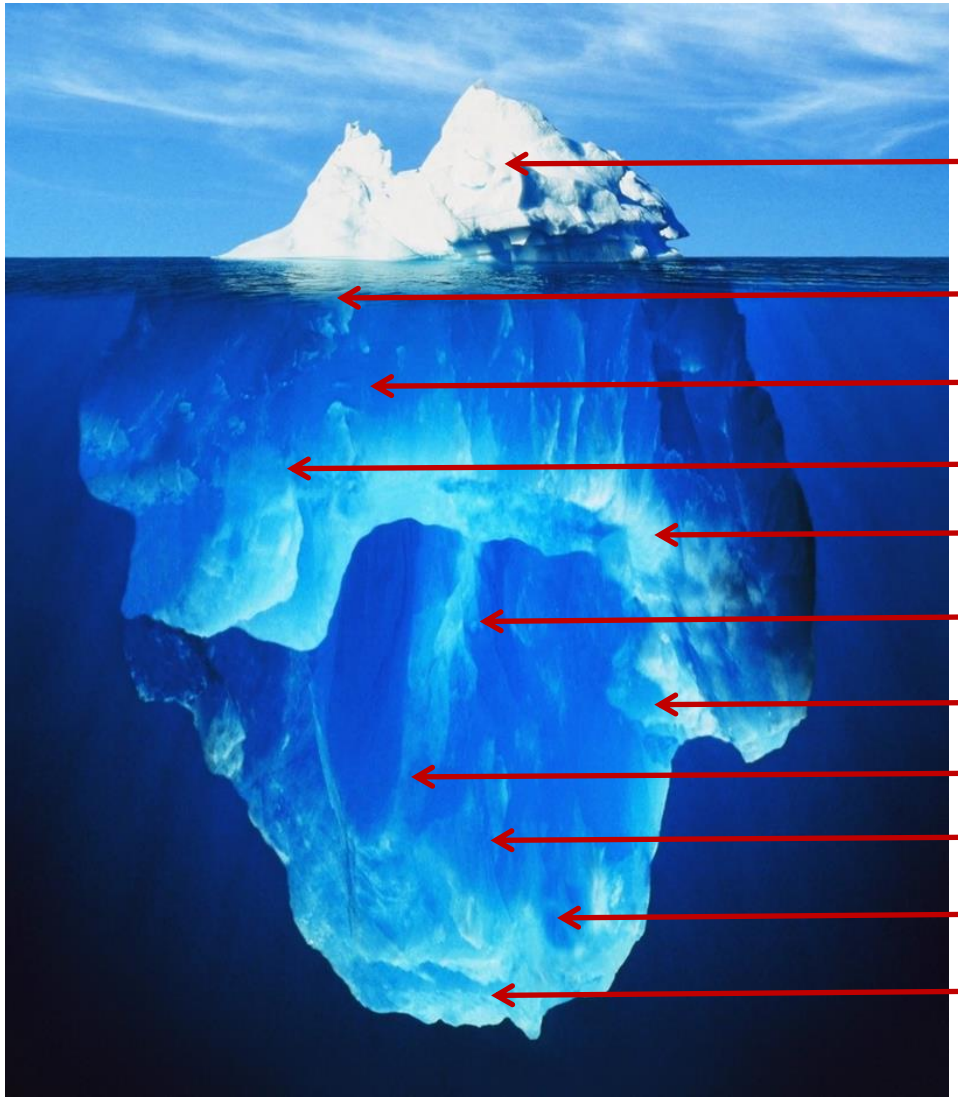

STROKE

Cerebral microbleeds

Hippocampal atrophy

White matter lesions

Oxidative stress

Chronic Hypoperfusion

Amyloidopathy

CNS inflammation

Mitochondrial dysfunction

Dysfunctional neurotransmitter systems

Disturbed lipid metabolism

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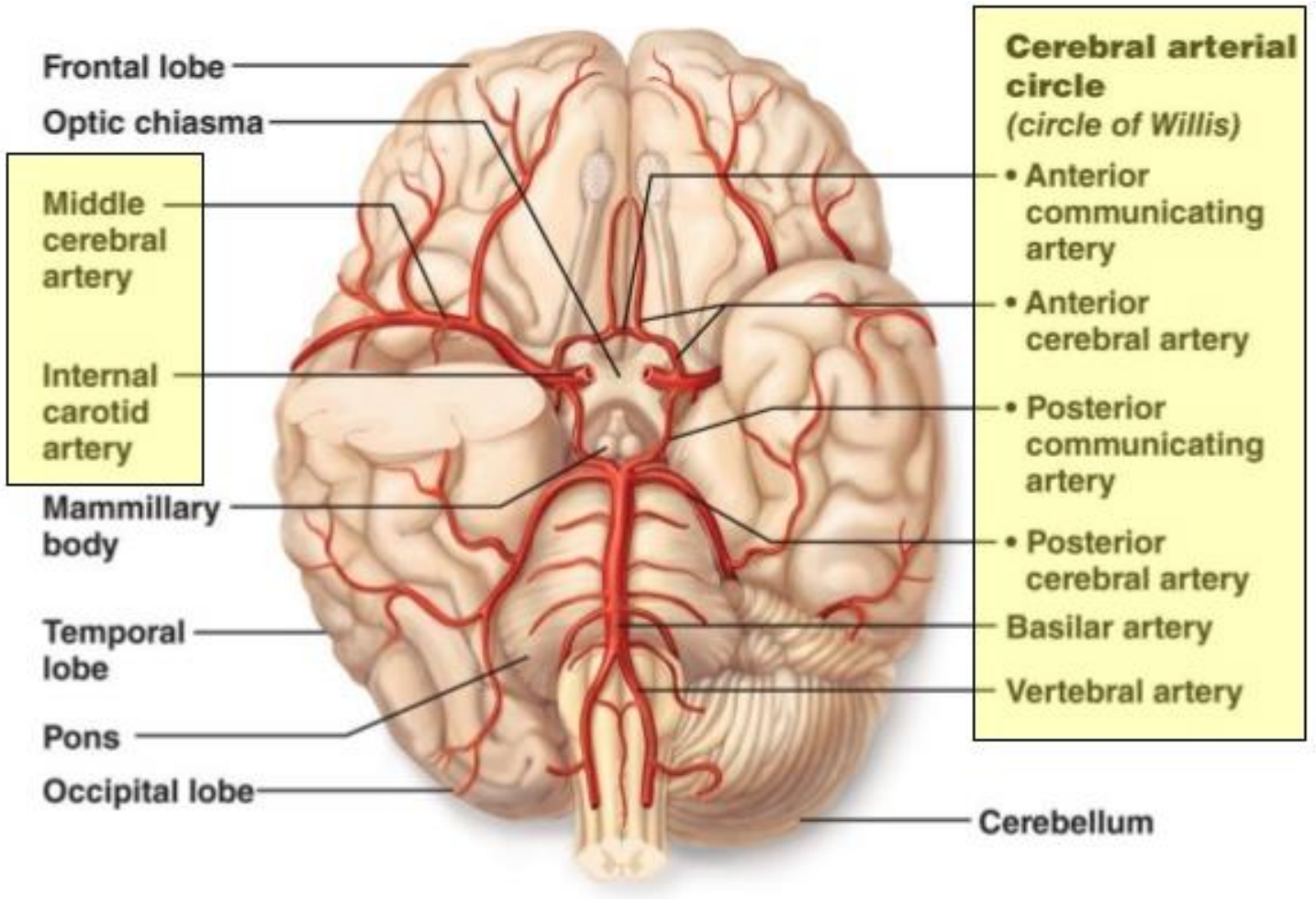
# Factors contributing to the presentation of PSD

- Location of the stroke → type/s of impairment
- Volume of the stroke → degree of impairment
- Degree of related neuronal or WM damage
- Presence of other cerebral pathology (e.g. Aβ or CAA)
- Presence of pre-existing cognitive impairment

# Location, location, location

**MCA strokes can affect the frontal, temporal, & parietal lobes**

**ICA strokes can affect the frontal, temporal, parietal, or occipital lobes, as well as the basal ganglia & thalamus**




**ACA & ACoA strokes can affect the frontal & possibly the parietal lobes**

**PCA strokes can affect the parietal lobes, thalamus, brain stem, & cranial nerves associated with eye movement**

Adapted from BNI Stroke Education Manual, 2015

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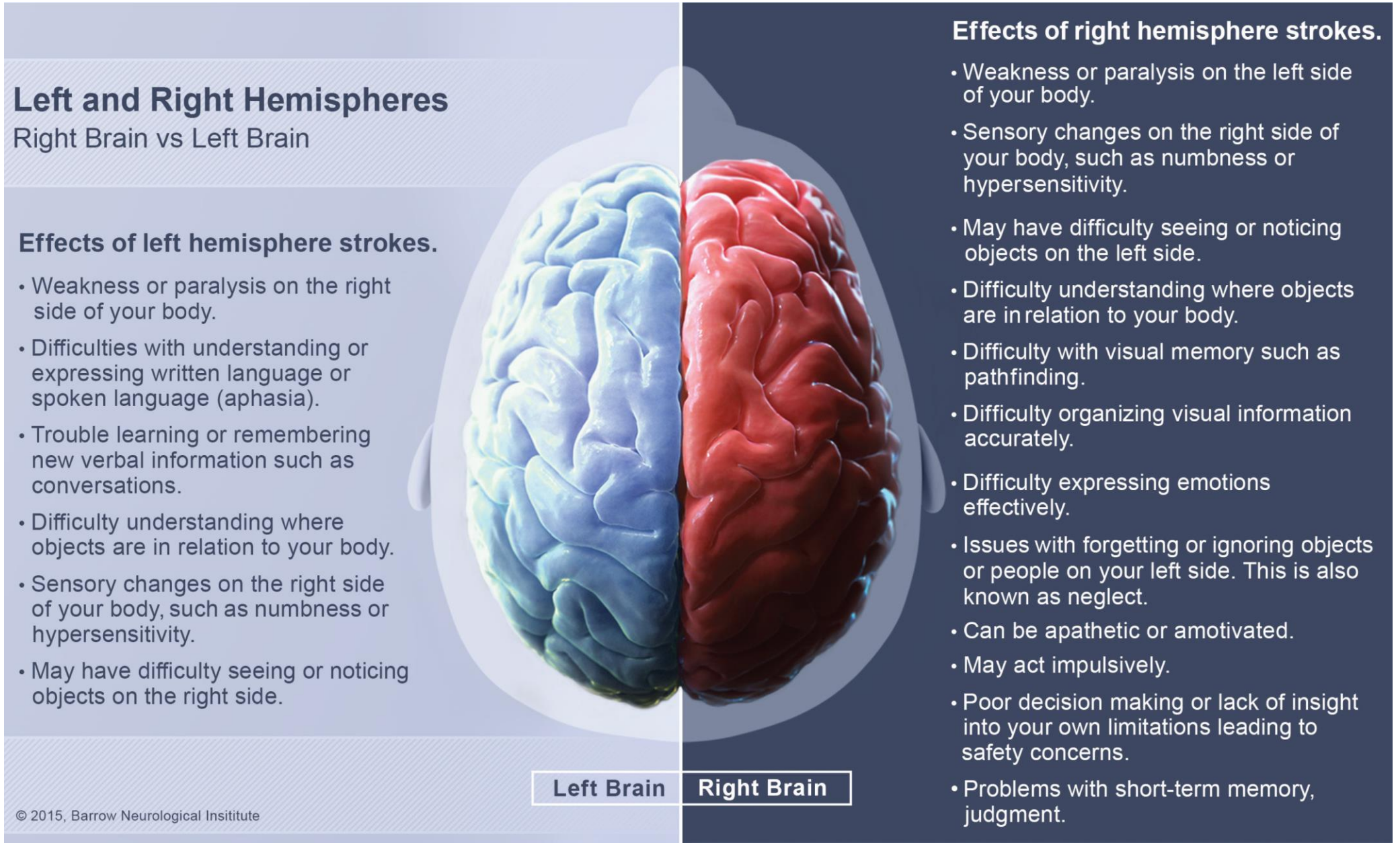
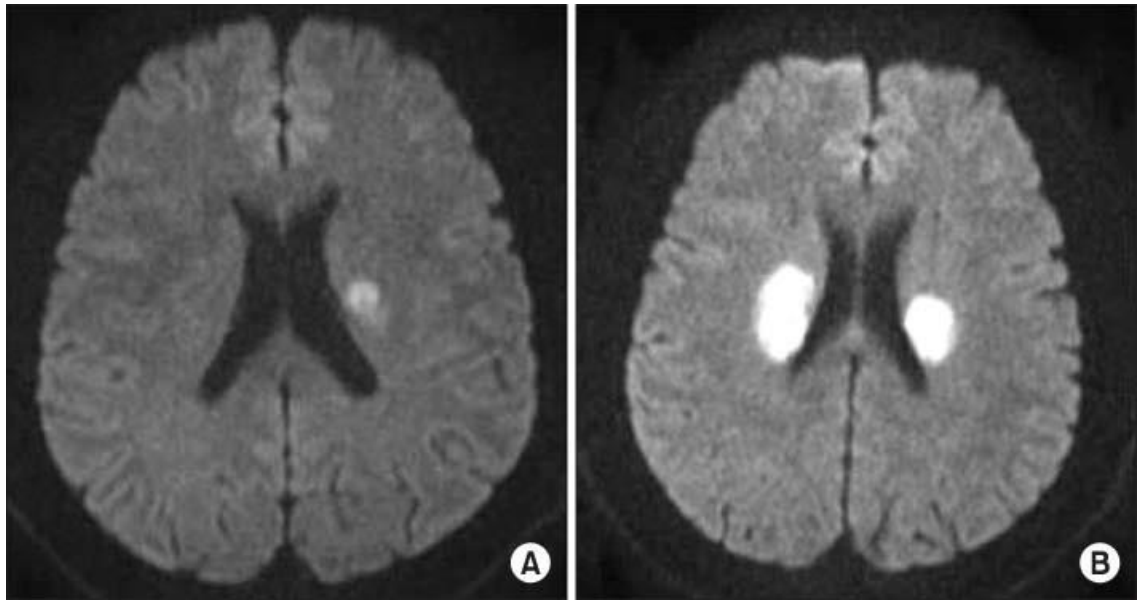



Image from BNI Stroke Education Manual, 2015

# Location: Strategic Infarcts

- A single small infarct may cause severe deficits when located in a strategic brain region
- Most strategic locations integrate into larger networks or cortical-subcortical loops




From Ji et al. *Brain Neurorehabil.* 2014

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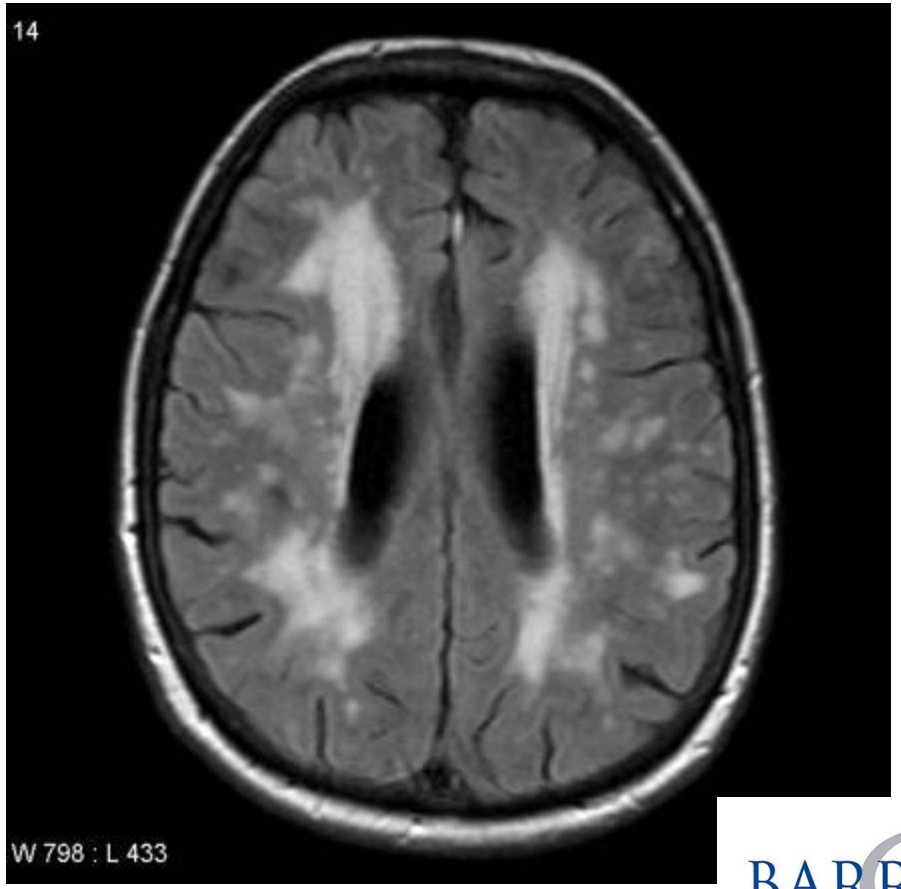
# Volume: Multi-infarct Dementia

- Larger infarct volumes &/or a higher number of smaller infarcts are associated with worse cognition & higher dementia risk (Schneider et al. *Neurology.* 2003)

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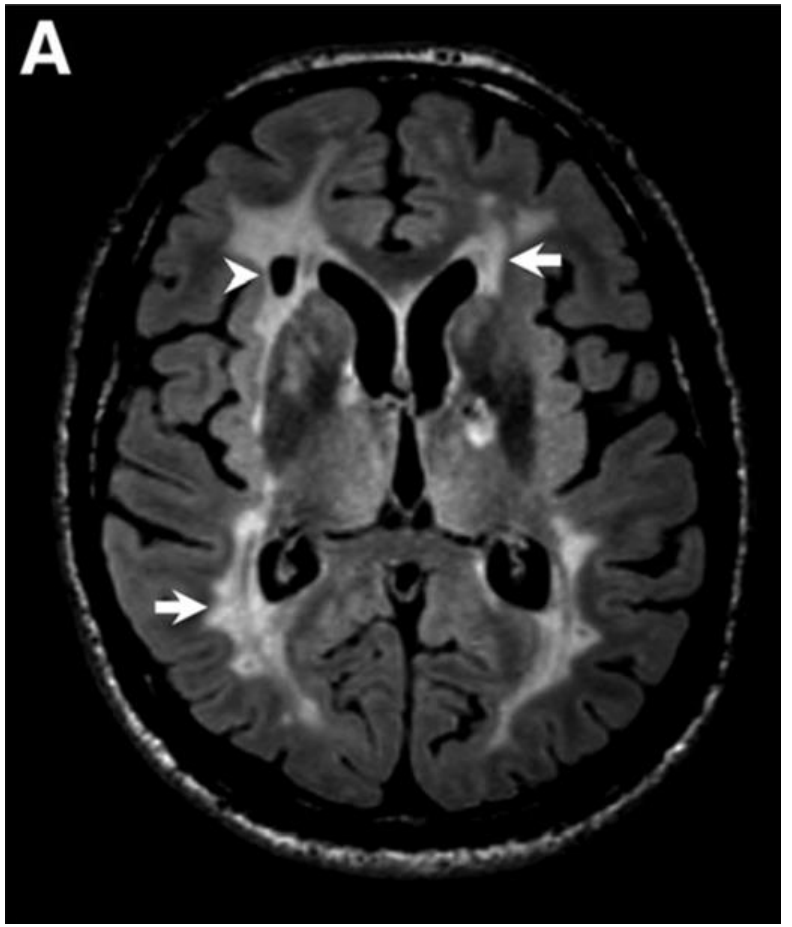
# White Matter Lesions: Subcortical Ischemic VaD

- Microvascular ischemic disease is associated with lacunar infarct & both are associated with risk of PSD (Pantoni L., *Lancet Neurol.* 2010)




From: Dichgans & Leys *Circulation Res. 2017.*

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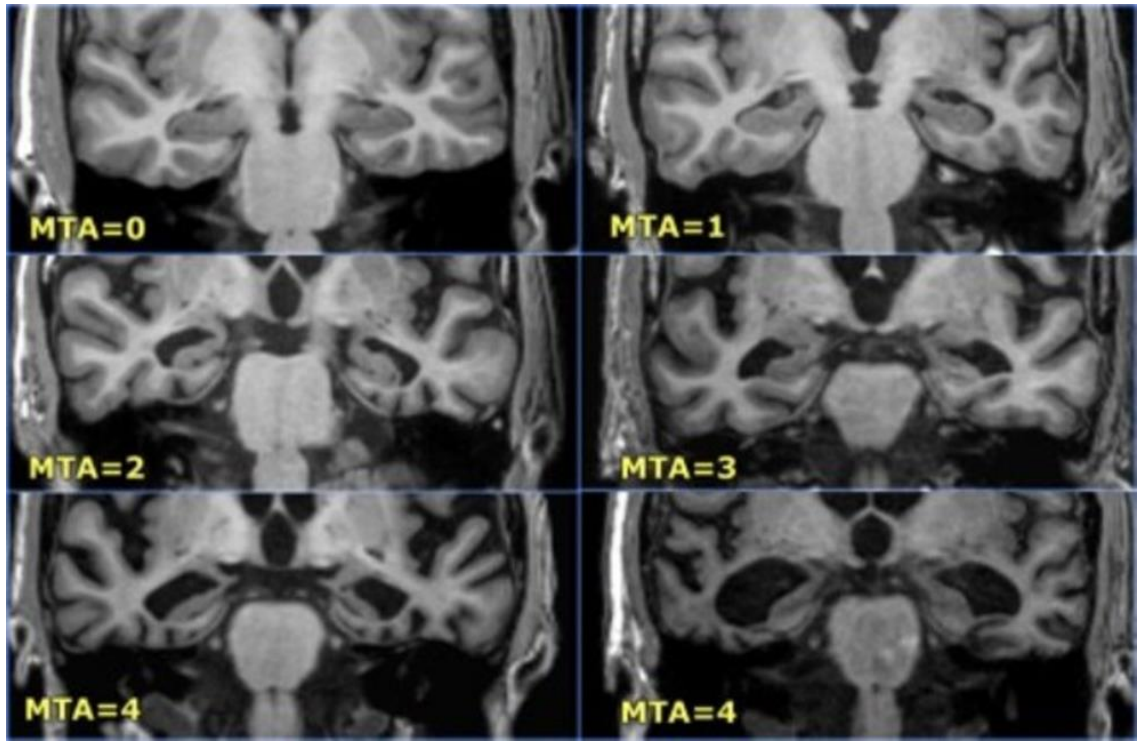
# Pre-existing Pathology: AD

- Vascular risk factors may lead to hippocampal atrophy & raise risk of stroke
- Brain infarcts are associated with smaller hippocampi; both are independently associated with memory decline (Blum et al., *Neurology* 2012)

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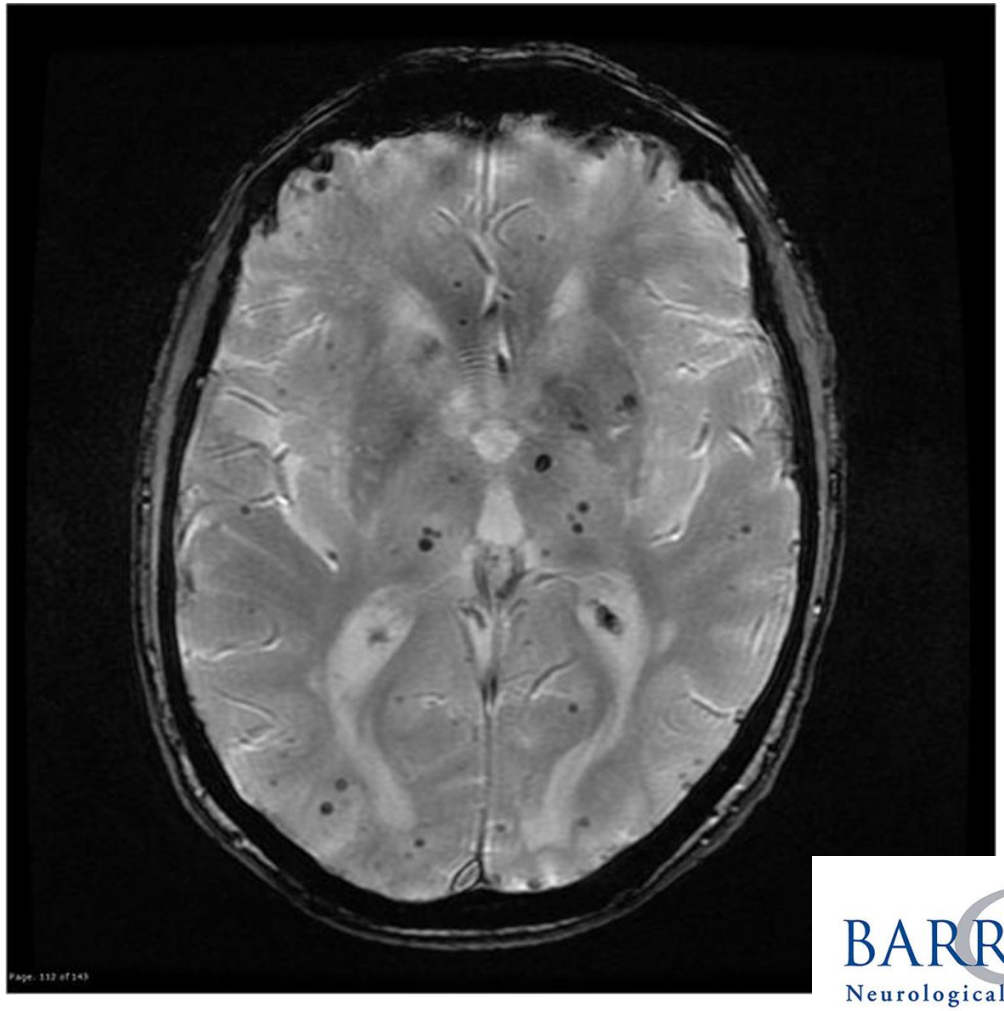
# Cerebral Pathology: Cerebral Angiopathy

- Accumulation of cerebral amyloid-β (Aβ) in cortical vessels of the brain
- Along with AD it is a common cerebral amyloid deposition disease



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# Summary: Diagnosis of PSD

| | | |
|---|---|---|
| Imaging | CT scan | Identifies strokes & hemorrhages |
| | MRI | |
| | CT angiography | Identifies aneurysms, AVMs, & other vessel abnormalities |
| | MRI angiography | |
| | Angiogram | |
| | Echocardiogram | Identifies blood clots & assesses blood flow through the heart |
| Lab work | Blood tests | Identifies vascular risk factors (e.g., HLD, DM2, clotting disorder) |
| Neuropsychological evaluation | Cognitive Tests | Identifies cognitive impairment |
| | Functional Tests | Identifies functional impairment |

# Summary: Complications of PSD Diagnosis

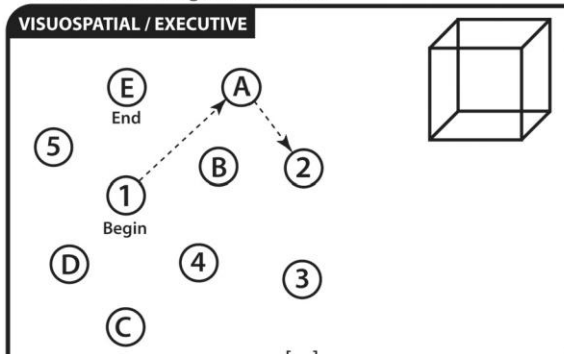
- Failure to exclude individuals with undiagnosed cognitive decline prior to stroke
- Overlap of PSD/VaD and other dementias (e.g. AD)
- Overlap of PSD & post stroke mood disorder
- Heterogeneity of test batteries
  - Beside testing (e.g. MMSE; MoCA) vs Comprehensive NP testing
- Heterogeneity of samples
  - National differences
  - Ethnic differences
  - Genetic differences
  - Age/education differences
  - Duration since stroke

# Neuropsychological evaluation after stroke

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

**VISUOSPATIAL / EXECUTIVE** — POINTS




Copy cube



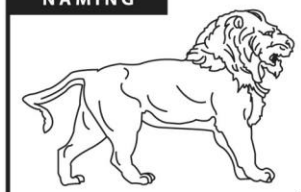
[ ] [ ]

Draw CLOCK (Ten past eleven)
( 3 points )

[ ] Contour [ ] Numbers [ ] Hands

__/5

**NAMING**



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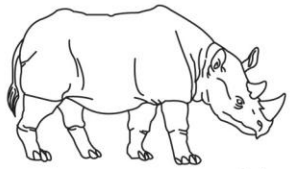

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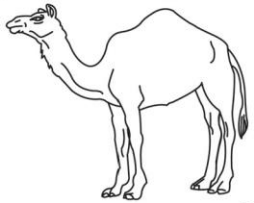

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**MEMORY** — Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

| | FACE | VELVET | CHURCH | DAISY | RED |
|---|---|---|---|---|---|
| 1st trial | | | | | |
| 2nd trial | | | | | |

No points

**ATTENTION** — Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

**LANGUAGE** — Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

__/1

**ABSTRACTION** — Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

**DELAYED RECALL**

| | Has to recall words WITH NO CUE | FACE | VELVET | CHURCH | DAISY | RED | Points for UNCUED recall only |
|---|---|---|---|---|---|---|---|
| | | [ ] | [ ] | [ ] | [ ] | [ ] | |
| **Optional** | Category cue | | | | | | |
| | Multiple choice cue | | | | | | |

__/5

**ORIENTATION** [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

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Normal ≥ 26 / 30

TOTAL __/30

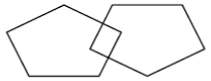
Add 1 point if ≤ 12 yr edu

Administered by: _____

# Mini-Mental State Examination (MMSE)

Patient's Name: _____ Date: _____

***Instructions:* Ask the questions in the order listed. Score one point for each correct response within each question or activity.**

| Maximum Score | Patient's Score | Questions |
|---|---|---|
| 5 | | "What is the year? Season? Date? Day of the week? Month?" |
| 5 | | "Where are we now: State? County? Town/city? Hospital? Floor?" |
| 3 | | The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____ |
| 5 | | "I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …) Stop after five answers.<br>Alternative: "Spell WORLD backwards." (D-L-R-O-W) |
| 3 | | "Earlier I told you the names of three things. Can you tell me what those were?" |
| 2 | | Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them. |
| 1 | | "Repeat the phrase: 'No ifs, ands, or buts.'" |
| 3 | | "Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.) |
| 1 | | "Please read this and do what it says." (Written instruction is "Close your eyes.") |
| 1 | | "Make up and write a sentence about anything." (This sentence must contain a noun and a verb.) |
| 1 | | "Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)<br>  |
| 30 | | TOTAL |

(Adapted from Rovner & Folstein, 1987)

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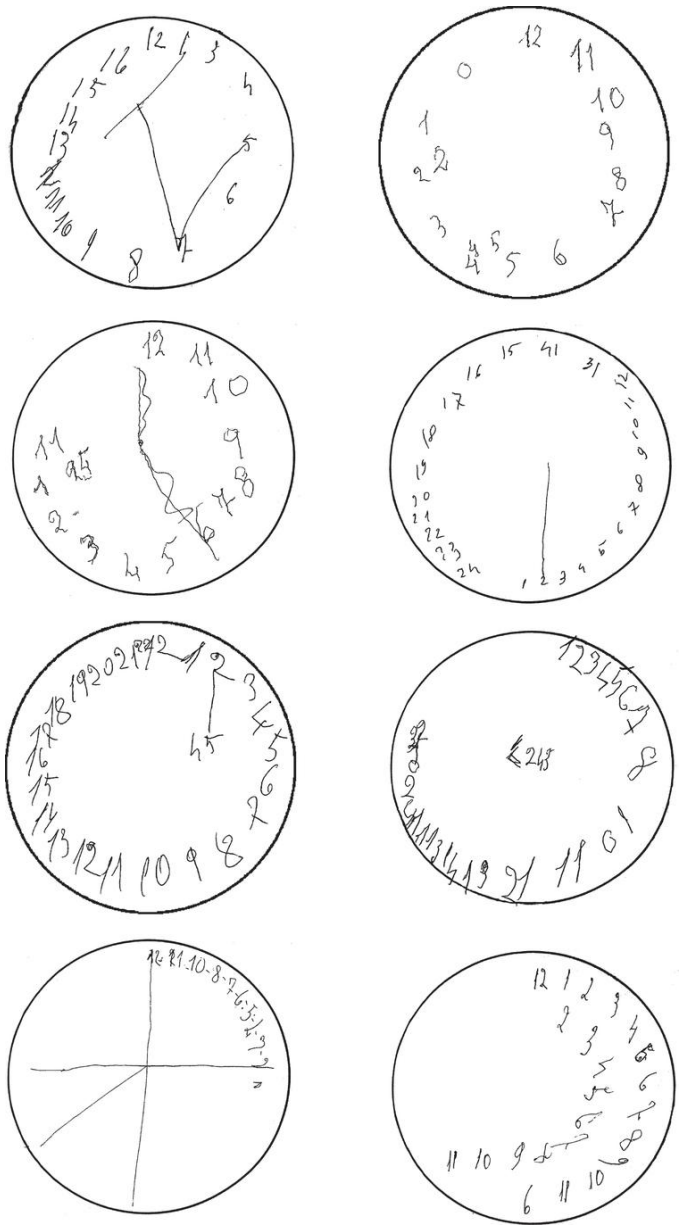
# “Set the time to 2:45”

Alzheimer’s disease
Spatial distortions & errors of impaired semantic knowledge

Vascular dementia
Planning errors, perseverations, & stimulus-bound responses

Frontotemporal lobar dementia
Planning errors, perseverations, & stimulus-bound responses

Lewy body dementia
Gross spatial distortions and perseverations



Luigi & Guido, *J of Alz Dis*, 2016

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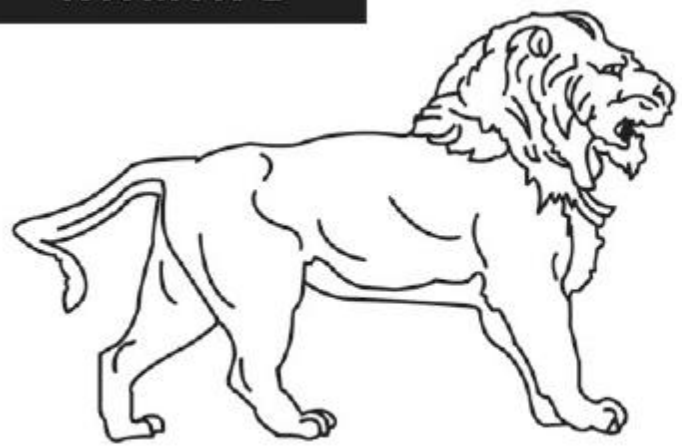
## NAMING



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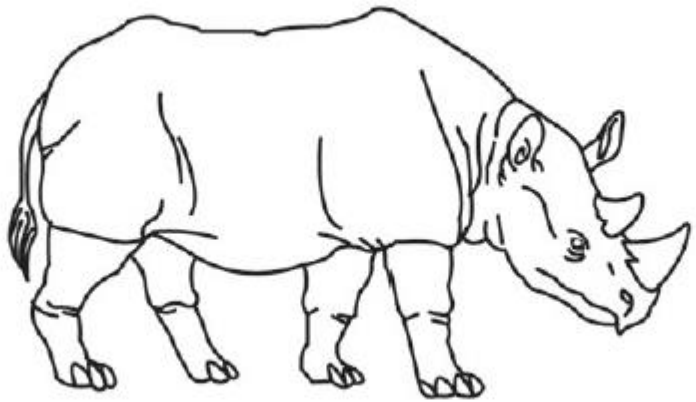

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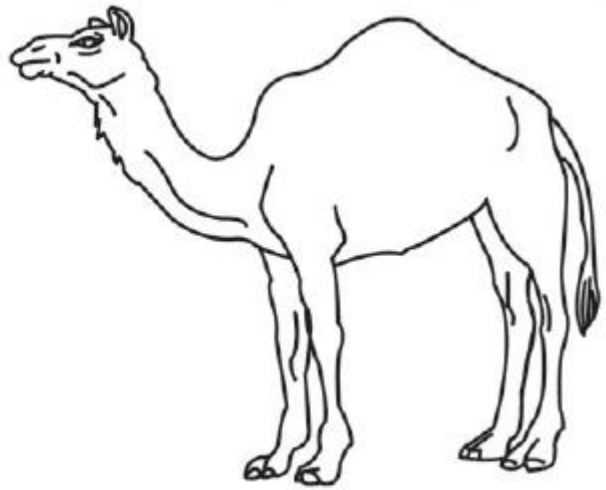

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **MEMORY** Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes. | | FACE | VELVET | CHURCH | DAISY | RED | No points |
| | 1st trial | | | | | | |
| | 2nd trial | | | | | | |
| **ATTENTION** Read list of digits (1 digit/ sec.). | Subject has to repeat them in the forward order [ ] 2 1 8 5 4 | | | | | | ___/2 |
| | Subject has to repeat them in the backward order [ ] 7 4 2 | | | | | | |
| Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B | | | | | | | ___/1 |
| Serial 7 subtraction starting at 100 | [ ] 93 | [ ] 86 | [ ] 79 | [ ] 72 | [ ] 65 | | ___/3 |
| | 4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** | | | | | | |

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| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words) | | | | | | | | __/1 |
| **ABSTRACTION** | Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler | | | | | | | __/2 |
| **DELAYED RECALL** | Has to recall words **WITH NO CUE** | FACE [ ] | VELVET [ ] | CHURCH [ ] | DAISY [ ] | RED [ ] | Points for UNCUED recall only | __/5 |
| **Optional** | Category cue | | | | | | | |
| | Multiple choice cue | | | | | | | |
| **ORIENTATION** | [ ] Date | [ ] Month | [ ] Year | [ ] Day | [ ] Place | [ ] City | | __/6 |



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Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

| A Typical Neuropsychological Test Battery | |
|---|---|
| Intellectual Ability | • Estimated premorbid FSIQ (demographics + word reading)<br>• Verbal abilities vs spatial abilities (lateralization)<br>• Abstract vs concrete response style |
| Attention & Working Memory | • Attention span (digits forward)<br>• Divided & Complex attention (working memory)<br>• Sustained attention |
| Processing Speed | • Target cancellation, Visual scanning & sequencing<br>• Motor speed<br>• Oral vs manual speed |
| Executive Function | • Verbal fluency: semantic vs phonemic retrieval<br>• Verbal vs Design fluency (lateralization)<br>• Card sorting: deductive reasoning |
| Language & Visuospatial Skills | • Naming: word finding ability<br>• Visuoconstruction: visual defects, organizational strategies |
| Learning & Memory | • Verbal vs nonverbal<br>• Encoding vs retrieval vs recognition |
| Mood & Functional Ability | • Mood disorder<br>• Functional independence |

# Mood Disorder

- In a recent meta-analysis of post-stroke MDD, the point prevalence of depression was 17.7% (95% CI = 15.6% to 20.0%) (Mitchell et al., *Gen Hosp Psychiatry* 2017)
  - 15.8% in outpatient settings and 20.0% in rehabilitation settings
  - An additional 3.1% had dysthymia and 6.9% had adjustment disorder
- The relative risk of MDD was 50% higher and the relative risk of any depressive disorder was 26% higher following left (dominant) hemisphere stroke.
  - The relative risk of any depressive disorder was 50% higher following aphasia
- Family history of mood disorder and personal history of prior mood disorder also increased risk of PSD

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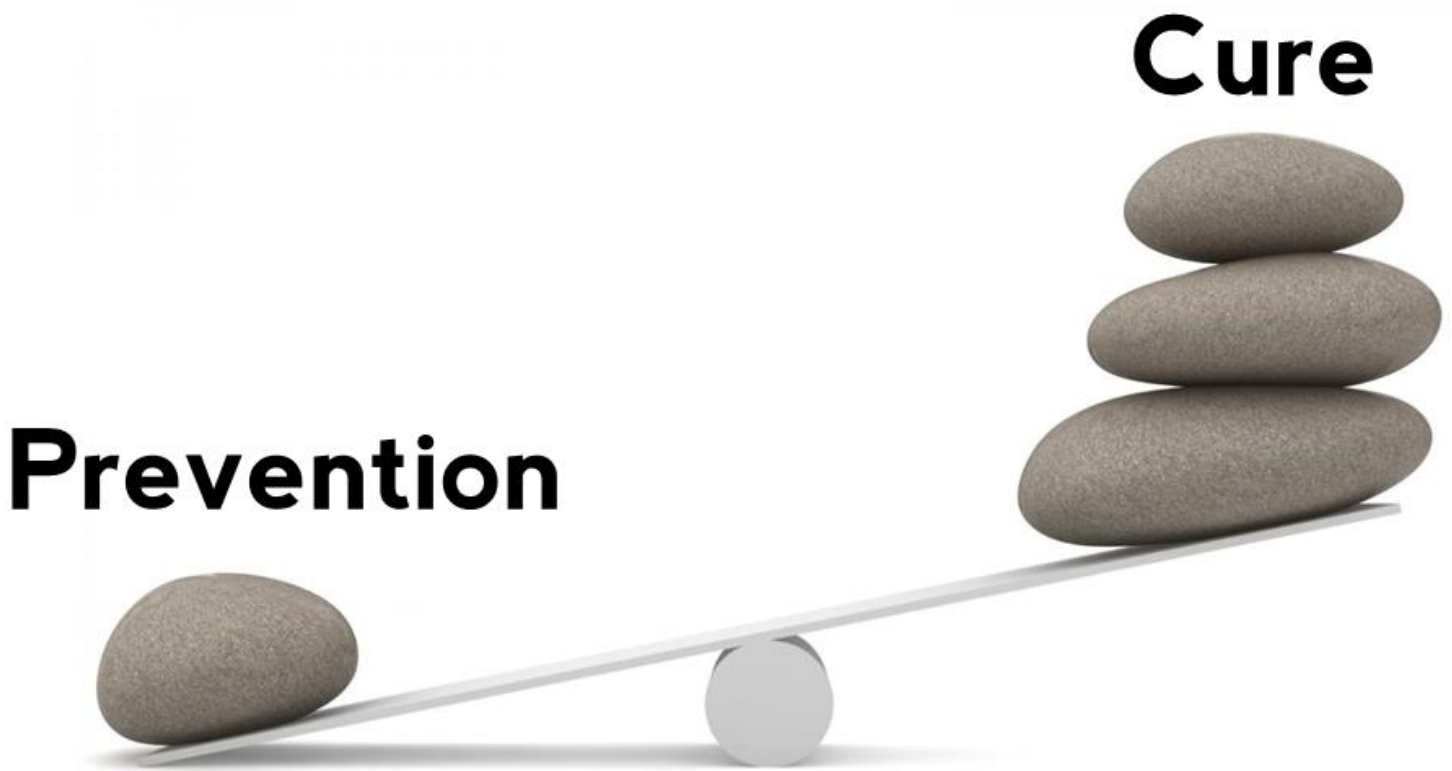
# Measures of Functional Independence

- Texas Functional Living Scale (TFLS): Requires that the patient demonstrate practical skills necessary for IADLs
- IADLs questionnaire: Best used as a caregiver report; provides a valuable second opinion regarding functional independence
- Test of Practical Judgment (TOP-J): Measures subjective decision-making in a variety of circumstances

# Intervention

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# Before Stroke: Management of Vascular Risk Factors

- Prevent the development of vascular risk factors
  - Patient education
  - Diet & exercise
  - Consultation with nutritionists
  - Eliminate tobacco use
  - Minimize alcohol use
- Adequately manage risk factors that emerge
  - Same as above, with the addition of medication
    - Anti-hypertensives
    - Anti-platelet therapy
    - Statins
    - Metformin/insulin

# After stroke: Rehab therapies

## Inpatient

- Acute care: 24-hour hospital based medical care; therapies as ordered by physician
- Inpatient Rehab: 24-hour care with at least 3 hours of therapy per day
- Skilled Nursing: daily nursing care, less demanding therapy but longer stay
- Long-term Care: long-term nursing care with limited rehab

## Outpatient

- Outpatient Rehab: 1-2 hour sessions several times a week
- Home Health Care: Nursing + 1-2 hour sessions several times a week
- Adult Day Care: Nursing, no therapies provided
- Group Home: Limited nursing, therapies as ordered by physician
- Assisted Living: Limited nursing, no therapies

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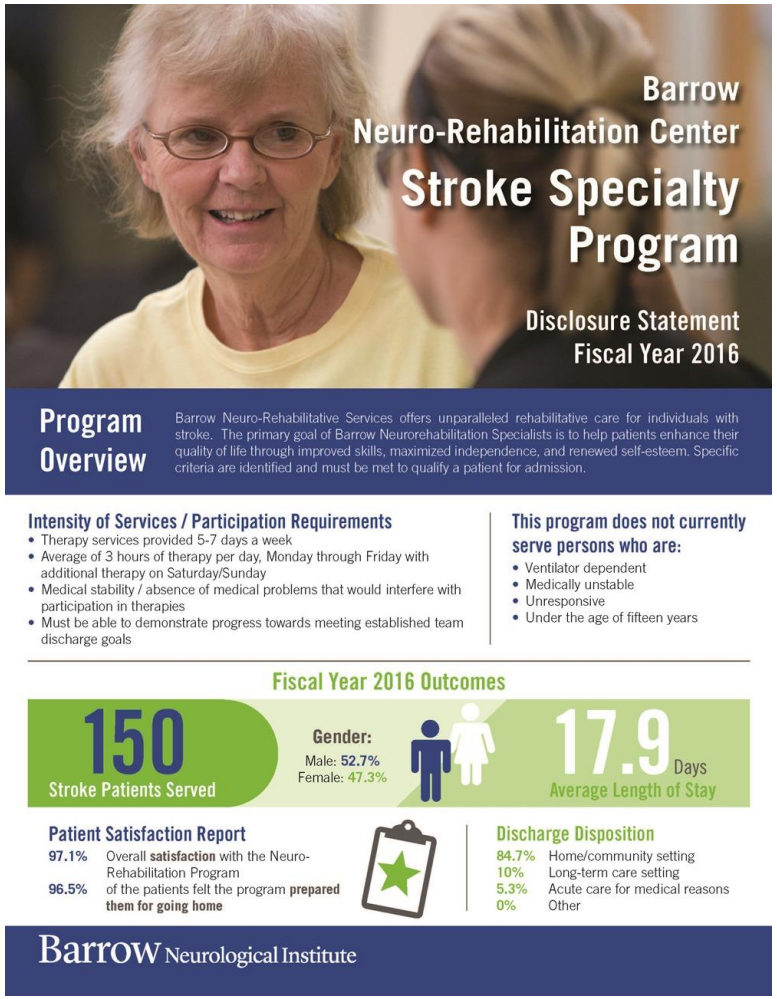
Adapted from BNI Stroke Education Manual, 2015

# Holistic Neuro-Rehabilitation

- Multimodal treatment approach
- PT, OT, Speech & therapies
  - Adjuvant therapies such as Botox
  - Education on future stroke prevention
  - Training in compensatory strategies
  - Support groups for mood and adjustment disorders

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# BNI Center for Transitional Neuro-Rehabilitation

- Transitional Neuro-rehabilitation
  - Helps individuals transition back to work, school, or the community
  - Team helps patient set personal goals & build skills important to their unique circumstances
- Programs offered at the BNI Center for Transitional Neuro-rehabilitation (CTN)
  - Home Independence Program
  - Work Reentry Program
  - School Reentry Program
  - Transitional Program
  - Refresher Program
  - Fast-Track Program

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# Supplements

- Citicoline (cytidine-5'-diphosphocholine)
  - Some evidence suggests citicoline improves post-stroke cognition compared to placebo (Cotroneo et al., *Clin Interv Aging* 2013)
- Ginko biloba
  - Studies of GB have suggested improvement in cognitive function and IADLs in AD & VaD after 24+ weeks of treatment (Ihl et al., *Pharmacopsychiatry* 2012; and Zhang et al. *Asian Pac J Trop Med* 2012).


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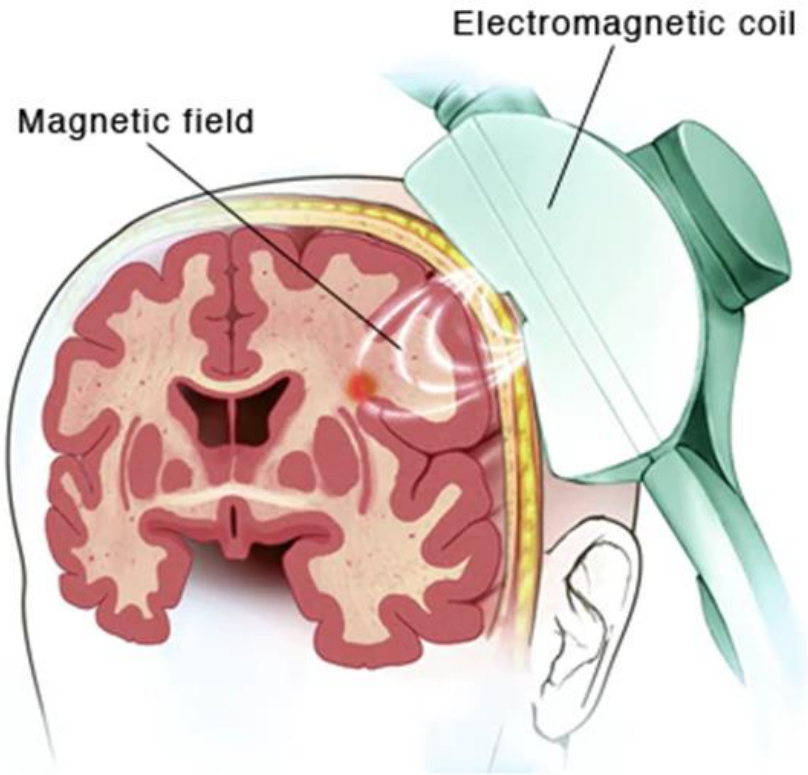
# Non-pharmacological Treatments

- Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS)
  - Several studies have shown that TMS might improve cognitive performance.
  - In AD, effects are likely mediated by compensatory mechanisms supporting residual abilities; similar plastic phenomena are invoked in VaD.





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# Disease Modifying Therapies

- A disease modifying therapy aims to change the natural course of an illness, usually a chronic disease, e.g. neurodegenerative & neuroinflammatory diseases
- Like remitting neurodegenerative diseases, PSCI and VCI:
  - Have a preclinical phase
  - Have acute episodes with a gradual evolution of functional deficits
  - In older patients, VCI or PSCI are often combined with AD-type pathology that contributes to the evolution and provides other targets for a disease-modifying strategy

Bordet et al. *BMC Medicine* 2017

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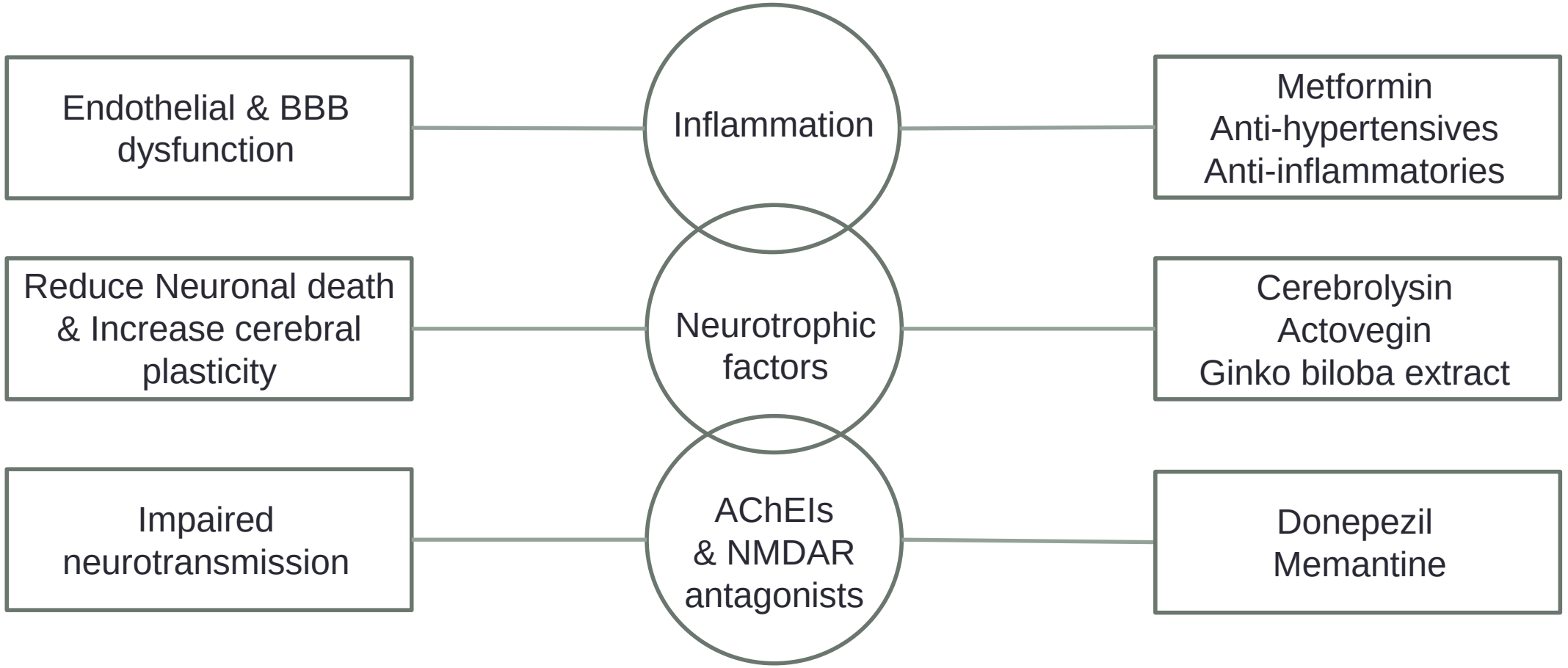
# Targets of DMTs




Bordet et al. *BMC Medicine* 2017

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# Potential pitfalls of DMTs

- Addressing the wrong target
- Interfering with the target pathology outside the window of opportunity
- Patients lacking the target pathology
- Choosing insensitive outcomes

Bordet et al. *BMC Medicine* 2017

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# In conclusion

- Vascular risk factors are increasing & survival after stroke is improving, leading to increased prevalence of PSCI and PSD
- Especially in older adults, PSCI and PSD often occur in conjunction with pre-existing vascular risk factors and/or occult neurodegenerative disease, complicating diagnosis
- Comprehensive neuropsychological assessment can help determine degree of impairment, identify other possible etiological contributors, and provide treatment recommendations
- Typical interventions include controlling risk factors to prevent future stroke & rehab therapies
- DMTs present a novel pathway for intervention

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Thank you for your attention.