Cognitive Decline: Pharmacologic Treatments

DMTs have demonstrated positive effects on cognition in clinical trials or observational studies

- **Alemtuzumab:** ↓patients demonstrating impaired CPS[1]
- **Glatiramer acetate:** BICAMS scores significantly improved relative to placebo[2]
- **Interferon β-1a:** Proportion of patients with cognitive impairment (on ≥3 cognitive tests) steady over 5 years; protective effect greater in women than men[3]
- **Interferon β-1b:** Improved complex attention, concentration, visual learning, recall, BICAMS scores[2,4]
- **Natalizumab:** ↑attention, memory, executive function[2]
- **Ocrelizumab:** Associated with stable or improved SDMT and BVMT-R scores in most patients after 1 year[5]
- **Siponimod:** ↓risk of decreased CPS relative to placebo; sustained in long-term follow-up[6]

BICAMS: Brief International Cognitive Assessment; BVMT-R, Brief Visuospatial Memory Test – Revised; CPS, cognitive processing speed; DMT, disease-modifying therapy; SDMT, Symbol Digit Modalities Test.

1. Riepl E et al. *Front Neurol*. 2018;8:730; 2. Miller E et al. *Curr Neuropharmacol*. 2018;16:475-483; 3. Patti F et al. *PLoS One*. 2013;8:e74111;
4. Barak Y et al. *Eur Neurol*. 2002;47:11-14; 5. Benedict R et al. *Neurology*. 2022;98(18 Supplement):647. Abstract P1-1 Virtual; 6. Cree BA et al. *Mult Scler*. 2022;28:1591-1605.

Cognitive Decline: Alzheimer Treatments

Alzheimer drugs **not** recommended for MS: lack of efficacy and risk of neurologic side effects[1-3]

- **Memantine**
  - NMDA antagonist
  - Of clinical interest because of glutamate involvement in MS pathophysiology[1]
- **Donepezil**
  - AChE inhibitor
  - Of clinical interest because anticholinergic lesions are associated with impaired memory in MS[2,3]

AChE, acetylcholinesterase. NMDA, N-methyl-D-aspartate.

1. Turalde CWR et al. *Front Neurol*. 2021;11:574748; 2. Krupp LB et al. *Neurology*. 2011;76:1500-1507; 3. Miller E et al. *Curr Neuropharmacol*. 2018;16:475-483.

Cognitive Decline: Nonpharmacologic Treatments

RCTs found significant cognitive benefits in MS, using

- Restorative training
  - Repetitive training for targeted cognitive functions, such as CPS or working memory
  - Computer-based, in clinic or at home
  - Significant improvements in attention, CPS, executive function, memory
  - Cognitive improvements correlate with changes in brain activity and functional connectivity
  - Benefits have persisted up to 2 years, but not in all studies
- Compensatory strategies
  - Use mental imagery, contextual clues, musical mnemonics, and other strategies to retain information
  - Improved memory
  - Associated with increased brain activity and functional connectivity

CPS, cognitive processing speed; RCT, randomized controlled trial.

Benedict R et al. *Lancet Neurol.* 2020;19:860-871.