

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Rao SM, Leo GJ, Bernardin L, et al. Cognitive dysfunction in multiple sclerosis: I. Frequency, patterns, and prediction. *Neurology* 1991; 41: 685–691.
2. Langdon DW. Cognitive impairment in multiple sclerosis—recent advances and future prospects. *Eur Neurol Rev* 2010; 5: 69–72.
3. Morrow SA, Jurgensen S, Forrestal F, et al. Effects of acute relapses on neuropsychological status in multiple sclerosis patients. *J Neurol* 2011; 258(9): 1603–1608.
4. Benedict RH, Morrow S, Rodgers J, et al. Characterizing cognitive function during relapse in multiple sclerosis. *Mult Scler* 2014; 20(13): 1745–1752.
5. Benedict RH, Pol J, Yasin F, et al. Recovery of cognitive function after relapse in multiple sclerosis. *Mult Scler* 2021; 27(1): 71–78.
6. Giedraitiene N and Kaubrys G. Distinctive pattern of cognitive disorders during multiple sclerosis relapse and recovery based on computerized CANTAB tests. *Front Neurol* 2019; 10: 572.
7. Foong J, Rozewicz L, Quaghebeur G, et al. Neuropsychological deficits in multiple sclerosis after acute relapse. *J Neurol Neurosurg Psychiatry* 1998; 64(4): 529–532.
8. Pardini M, Uccelli A, Grafman J, et al. Isolated cognitive relapses in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2014; 85(9): 1035–1037.

Visit SAGE journals online
journals.sagepub.com/
home/msj

 SAGE journals

Do isolated cognitive relapses exist? Commentary

Aurélie Ruet 

Cognitive impairment is frequent in patients with multiple sclerosis (PwMS). The cognitive deficits could worsen along the disease contributing to significant disability taking into account some heterogeneity among PwMS. However, the possibility of acute cognitive change has been reported during relapse, which includes physical symptoms, with full or partial recovery.^{1–3} Besides, the concept proposed by Pardini et al.⁴ relating to ‘Isolated Cognitive Relapses’ (ICRs) – with no physical worsening – based on a transient decrease of the Symbol Digit Modalities Test (SDMT) in PwMS is debated. The SDMT assessing mainly information processing speed has been well validated in MS, and its clinically meaningful change has been proposed based on ecological endpoint.⁵ Nevertheless, Pardini et al.⁴ acknowledged some limitations concerning the choice of this definition of ICRs only based on one neuropsychological (NP) assessment. They underlined that ICRs were not self-identified, but they highlighted the value of informant versions of the Multiple Sclerosis Neuropsychological Screening Questionnaire (MSNQ).⁶ Interestingly, Pardini et al.⁴ also supported the clinical relevance of ICRs due to their association with cognitive daily functioning and further cognitive decline in PwMS.

Besides, Baldwin et al.⁷ emphasized that the data published by Pardini et al.⁴ came from retrospective study

with a small sample size. In fact, it could be unjustly concluded that ICRs do not exist, whereas they are simply under-recognized by both patients and physicians. Indeed, one could also wonder whether neurologists use some tools for identifying ICRs in practice. Importantly, baseline and follow-up relevant cognitive assessments are needed to be able to detect prospectively ICRs in clinical setting.

Moreover, cognitive impairment is driven by the cumulative brain inflammation and the ongoing neurodegeneration. It is questionable concerning the mechanisms leading to ICRs. The occurrence of new MS lesions in key and relevant areas involved in cognitive functions has been proposed for supporting them.⁴ One could argue that the presence of active inflammation could also alter the efficiency of brain networks and synaptic functioning that could drive a decrease of acute cognitive performance.⁸ The presence of gadolinium enhancing (Gd+) lesion is part of the definition of disease activity in MS, and has been used for supporting cognitive relapse.^{4,9} But the presence of Gd+ lesions only means the breakdown of blood–brain barrier, and does not reflect all types of inflammation within the brain. Most of the new grey matter lesions relevant for cognition are not identified, as well as diffuse inflammation and microglial activation that are not visualized with conventional imaging.

Multiple Sclerosis Journal

2021, Vol. 27(10) 1489–1490

DOI: 10.1177/

13524585211034123

© The Author(s), 2021.
Article reuse guidelines:
sagepub.com/journals-
permissions

Correspondence to:

A Ruet
Service de Neurologie, CHU
de Bordeaux, Place Amélie
Raba Léon, 33076, Bordeaux
Cedex, France
[aurelie.ruet@chu-
bordeaux.fr](mailto:aurelie.ruet@chu-bordeaux.fr)

Aurélie Ruet
Université de Bordeaux,
Neurocentre Magendie, U
1215 INSERM, Bordeaux,
France; Université de
Bordeaux, Service de
neurologie CHU de
Bordeaux, Bordeaux, France

So as defended by Baldwin, no large data could support the attractive concept of ICRs. Further longitudinal studies are required to confirm the presence and the relevance of ICRs in PwMS. This controversy underlines the absence of consensual definition of cognitive relapse, and highlights the importance of regular cognitive evaluations from the diagnosis of MS to the follow-up visits in clinical practice. These findings could help to disentangle this important question in the future, which could have prognostic and therapeutic implications for PwMS.


Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: A.R. reports personal fees and non-financial support from Novartis, personal fees and research grants from Biogen, personal fees and research grant from Roche, research grant from Genzyme, personal fees and research grant from Merck and research grant from Bayer, outside the submitted work.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

ORCID iD

Aurélie Ruet  <https://orcid.org/0000-0002-0020-8739>

References

1. Morrow SA, Jurgensen S, Forrestal F, et al. Effects of acute relapses on neuropsychological status in multiple sclerosis patients. *J Neurol* 2011; 258(9): 1603–1608.
2. Benedict RH, Morrow S, Rodgers J, et al. Characterizing cognitive function during relapse in multiple sclerosis. *Mult Scler* 2014; 20(13): 1745–1752.
3. Benedict RH, Pol J, Yasin F, et al. Recovery of cognitive function after relapse in multiple sclerosis. *Mult Scler* 2021; 27(1): 71–78.
4. Pardini M, Uccelli A, Grafman J, et al. Isolated cognitive relapses in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2014; 85(9): 1035–1037.
5. Benedict RH, DeLuca J, Phillips G, et al. Validity of the symbol digit modalities test as a cognition performance outcome measure for multiple sclerosis. *Mult Scler* 2017; 23(5): 721–733.
6. Meli R, Roccatagliata L, Capello E, et al. Ecological impact of isolated cognitive relapses in MS. *Mult Scler* 2020; 26(1): 114–117.
7. Baldwin C and Morrow S. Do isolated cognitive relapses exist? No. *Mult Scler* 2021; 27(10): 1488–1489.
8. Di Filippo M, Portaccio E, Mancini A, et al. Multiple sclerosis and cognition: Synaptic failure and network dysfunction. *Nat Rev Neurosci* 2018; 19(10): 599–609.
9. Bellmann-Strobl J, Wuerfel J, Aktas O, et al. Poor PASAT performance correlates with MRI contrast enhancement in multiple sclerosis. *Neurology* 2009; 73(20): 1624–1627.