

Echolalia: Paying attention to a forgotten clinical feature of primary
progressive aphasia

M. J. Torres-Prioris ^{a,b,c} and M. L. Berthier ^{a,b}

^a *Cognitive Neurology and Aphasia Unit (UNCA). Centro de Investigaciones Médico-Sanitarias (CIMES), University of Malaga, Malaga, Spain*

^b *Instituto de Investigación Biomédica de Málaga – IBIMA, University of Malaga, Málaga, Spain*

^c *Area of Psychobiology, Faculty of Psychology and Speech Therapy, University of Malaga, Malaga, Spain*

Keywords: echolalia, fronto-temporal dementia, language area, primary progressive aphasia, supplementary motor area

Correspondence: María José Torres-Prioris or Marcelo L. Berthier. Unidad de Neurología Cognitiva y Afasia. Centro de Investigaciones Médico-Sanitarias. Universidad de Málaga. Marqués de Beccaria 3, 29010. Málaga. España (tel: + 34 952137605, mjprioris@uma.es; mbt@uma.es).

DOI: 10.1111/ene.14712

One decade ago, the diagnostic criteria for three major forms of primary progressive aphasia (PPA) — nonfluent-agrammatic variant (nfvPPA), semantic variant (svPPA), and logopenic variant (lvPPA) — have been established based on expert consensus [1]. However, non-canonical forms of PPA (i.e., dynamic aphasia, pure apraxia of speech, pure anomia, dysprosodia) [2] and some features such as echolalia (repetition of what one has just heard) tend to be underestimated.

Cortical neurodegeneration in nfvPPA and lvPPA is respectively heightened in anterior and posterior regions of the left perisylvian speech-language network (PSLN) governing language repetition [1]. Involvement of the PSLN in nfvPPA and lvPPA mostly impairs sentence repetition [3,4] and might be a hindrance for the emergence of echolalia since this emanates from the uncontrolled activity of a relatively spared PSLN [5,6]. By contrast, the PSLN in the svPPA and in the behavioural variant of fronto-temporal dementia (bvFTD) is spared and this would explain why echolalia may frequently be observed in these two conditions. Mechanistically, echolalia in svPPA and in advanced stages of bvFTD occurs because neurodegeneration involving the anterior temporal and/or frontal cortices is ideally placed to “release” the activity of the anterior PSLN leading to verbal echoing [5,6].

The article by Ota and co-workers (this issue) [7] focused for the first time on the study of echolalia in a group of 45 PPA patients. The authors found echolalia in 12 patients with nfvPPA and in 2 patients with unclassified PPA. Patients with echolalia associated to nfvPPA were younger, had lower auditory comprehension scores, had variable performance on the repetition subtest of the Western Aphasia Battery (WAB) (score range: 3.1 - 9.9) and showed more imitation behaviour than those without echolalia. Notice that although the language disturbances in most nfvPPA were classified as anomic aphasia, the WAB does not distinguish amongst the three major forms of PPA [8]. Indeed, Ota’s finding of preserved repetition and echolalia in some nfvPPA patients was more akin to transcortical aphasias (two such patients actually had transcortical motor aphasia). The authors did find that all patients with verbal echoing had mitigated echolalia that they linked to faulty auditory comprehension and inhibitory control. More severe types of verbal echoing (automatic, effortful, echoing approval, and ambient) were not heard.

The diagnostic criteria for three major forms of primary progressive aphasia (PPA)—nonfluent-agrammatic variant (nfvPPA), semantic variant (svPPA) and logopenic variant (lvPPA)—were established a decade ago, based on expert consensus [1]. However, non-canonical forms of PPA (e.g., dynamic aphasia, pure apraxia of speech, pure anomia, dysprosodia) [2] and some features such as echolalia (repetition of what one has just heard) tend to be underestimated.

Cortical neurodegeneration in nfvPPA and lvPPA is heightened in anterior and posterior regions, respectively, of the left perisylvian speech-language network (PSLN) governing language repetition [1]. Involvement of the PSLN in nfvPPA and lvPPA mostly impairs sentence repetition [3,4] and might be a hindrance for the emergence of echolalia since this emanates from the uncontrolled activity of a relatively spared PSLN [5,6]. By contrast, the PSLN in the svPPA and in the behavioural variant of fronto-temporal dementia (bvFTD) is spared and this would explain why echolalia may frequently be observed in these two conditions. Mechanistically, echolalia in svPPA and in advanced stages of bvFTD occurs because neurodegeneration involving the anterior temporal and/or frontal cortices is ideally placed to “release” the activity of the anterior PSLN leading to verbal echoing [5,6].

The article by Ota and co-workers [7] focused for the first time on the study of echolalia in a group of 45 PPA patients. The authors found echolalia in 12 patients with nfvPPA and in two patients with unclassified PPA. Patients with echolalia associated to nfvPPA were younger, had lower auditory comprehension scores, had variable performance on the repetition subtest of the Western Aphasia Battery (WAB) (score range 3.1–9.9) and showed more imitation behaviour than those without echolalia. Notice that the language disturbances in most nfvPPA were classified as anomia suggesting that the WAB is not appropriate to distinguish between the three major forms of PPA, at least in the early stages [8]. Indeed, Ota et al.'s finding of preserved repetition and echolalia in some nfvPPA patients was more akin to transcortical aphasias (two such patients actually had transcortical motor aphasia). The authors did find that all patients with verbal echoing had mitigated echolalia that they linked to faulty auditory comprehension and inhibitory control. More severe types of verbal echoing (automatic, effortful, echoing approval and ambient) were not heard.

Since Ota and colleagues did not consider repetitive questions asked by patients to reinforce word meaning access as a form of mitigated echolalia, they probably overlooked its occurrence in their five patients with svPPA. Although it is admitted that sometimes it is difficult separating normal repetition from mitigated echolalia, elsewhere it has been argued that repetitive echoing of words and sentence fragments that sound ambiguous, equivocal or are poorly understood represent instances of mitigated echolalia in patients with svPPA [5,6]. For example, on the yes/no questions subtests of the WAB, when answering the question "Will paper burn in fire?" a woman with svPPA evaluated in our unit echoed some words, "The paper?... with the fire?... yes!", most likely to grasp their meaning. It has been suggested that instances of mitigated echolalia, like this, in patients with svPPA probably result from damage to the left inferior frontal-occipital fasciculus (ventral stream) in the anterior temporal lobe coupled with compensatory activity of the arcuate fasciculus (dorsal stream) and mirror neurons in the PSLN [5,6]. Anyhow, further studies on svPPA are required to demarcate the boundaries between normal repetition and mitigated echolalia.

Ota et al.'s study did not document echolalia in their seven patients with lvPPA. This may have been because echolalia was evaluated using unstructured, open-ended conversations in a small sample. It will be desirable in future studies to analyse echolalia using quantitative measures that allow correlation with the results of other linguistic and non-linguistic cognitive tests. Disease duration also needs to be controlled for. The lack of echolalia in lvPPA is intriguing since cases of mitigated echolalia coexisting or not with phonological approximations to the target word in production tasks have been reported in stroke patients with either conduction, Wernicke's or transcortical sensory aphasias due to left temporo-parietal lesions [5,6]. Nevertheless, more research is needed to unveil whether the same combination of these repetitive verbal behaviours can also occur in lvPPA.

Resting state functional neuroimaging with 123I-N-isopropyl-
p-iodoamphetamine single photon emission computed tomogra- phy (123I-

IMP-SPECT) in Ota et al.'s study revealed that echolalia was associated with lower bilateral regional perfusion rates in the pre-supplementary motor area, middle cingulate gyrus, dorsolateral prefrontal cortex, medial prefrontal cortex, anterior frontal operculum and thalamus. Therefore, dysfunction of such executive-control network induced echolalia in this sample of nfvPPA presumably by triggering automatic activation of action-perception circuits, including the mirror neuron system, in the PSLN [5,6]. In short, further studies, like the one by Ota and colleagues, are much needed to disentangle the occurrence and diagnostic relevance of verbal echoing in the different variants of PPA.

References

1. Gorno-Tempini ML, Hillis AE, Weintraub S, Kertesz A, Mendez M, Cappa SF et al. Classification of primary progressive aphasia and its variants *Neurology*. 2011; **76**(11):1006-1014.
2. Marshall CR, Hardy CJD, Volkmer A, et al. Primary progressive aphasia: a clinical approach. *J Neurol*. 2018; **265**: 1474-1490.
3. Forkel SJ, Rogalski E, Drossinos Sancho N, et al. Anatomical evidence of an indirect pathway for word repetition. *Neurology*. 2020; **94**: e594-e606.
4. Leyton CE, Savage S, Irish M, et al. Verbal repetition in primary progressive aphasia and Alzheimer's disease. *J Alzheimers Dis*. 2014; **41**: 575-585.
5. Torres-Prioris M, López-Barroso D, Roé-Vellvé N, Paredes-Pacheco J, Dávila G, Berthier ML. Repetitive verbal behaviors are not always harmful signs: Compensatory plasticity within the language network in aphasia. *Brain Lang*. 2019; **190**:16-30.
6. Berthier ML, Torres-Prioris MJ, López-Barroso D, et al. Are you a doctor? . . . Are you a doctor? I'm not a doctor! A reappraisal of mitigated echolalia in aphasia with evaluation of neural correlates and treatment approaches. *Aphasiology* 2018; **32**: 784-813.
7. Ota, S., Kanno, S., Morita, A., Narita, W., Kawakami, N., Kakinuma, K., ... & Nishio, Y. (2020). Echolalia in patients with primary progressive aphasia. *European Journal of Neurology*.
8. Clark HM, Utianski RL, Duffy JR, et al. Western Aphasia Battery–Revised Profiles in Primary Progressive Aphasia and Primary Progressive Apraxia of Speech. *Am J Speech Lang Pathol*. 2020; **29**: 498-510.