CAREFUL APPLICATION OF THE RECOMMENDED PROTOCOLS IMPROVE REPRODUCIBILITY AND PERMIT COMPARISON AMONG CCSVI STUDIES.

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Dear Editor,
We read with interest the article published by Rodger and Co-Authors "Evidence against the Involvement of Chronic Cerebrospinal Venous Abnormalities in Multiple Sclerosis. A Case-Control Study" (Plos One August 2013, Volume 8, Issue 8, e72495). As correctly reported, in 2009 we described the presence of chronic cerebrospinal venous insufficiency (CCSVI) in patients with multiple sclerosis (MS), proven by color Doppler ultrasonography (CDUS) and confirmed by catheter venography.[1] The results obtained by the Canadian researchers are exactly the antipodes of what we found, since they were unable to demonstrate any venous flow abnormalities in the MS patients investigated both with CDUS and MRV. We briefly discuss below, why the methodology adopted by the Authors may lead to a so strong discrepancy in comparing results.

i) Regarding CDUS methodology, we were very surprised that the Authors failed to use the updated methodology recently recommended by an international consensus in order to improve the reproducibility of the CDUS protocol.[2] The only meta analysis of all reports from 2005 till June 2011 demonstrated a strong prevalence of CCSVI in MS, but with marked heterogenicity among studies.[3] To avoid this and to make the studies more comparable after June 2011, seven international scientific societies developed a technically detailed protocol, not cited yet.[2,4]

ii) Contrary to the recommended protocol, we were impressed in the Rodger study by the absence of any M-mode analysis for investigating the criterion #3.[2] CDUS M-mode is indispensable to detect intraluminal obstacles and fixed valve leaflets, which represents the majority of CCSVI venous abnormalities.[4,5] In figure 1 the valve motility of a normal subject is well apparent as compared by a patient with CCSVI and MS. This represents an intraluminal obstacle leading to flow blockages and/or bidirectional flow depicted in the figure 2, and seen by several Authors, but, unfortunately, never detected in the survey reported by the Authors.[1-5]

iii) Regarding MRV methodology we were again surprised by the focus of the investigation in the upper and mid region of the neck, where significant differences in jugular flow rate where never detected in CCSVI condition. To the contrary, several reports measured significant restriction of the jugular flow rate, increased flow through the collaterals, and extraluminal stenosis in the lower portion of the neck, exactly where Rodger et al. omitted to perform any assessment.[6-15]

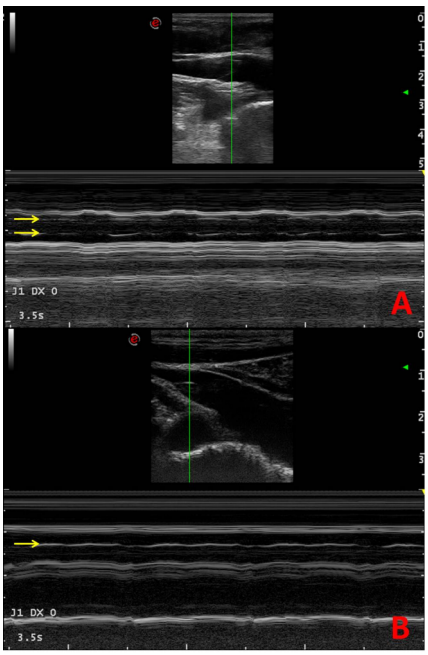

Figure 1. *A: Two mobile valve leaflets evidenced in the M-mode trace by the yellow arrows. The lumen is never occupied and both leaflets appears well saddled to the jugular vein wall.*
B: A fixed monocusp valve in a CCSVI case, where the yellow arrow indicate the occupancy of the center of the lumen. This constitutes an intraluminal obstacle generating the flow abnormalities represented in the lower panel of figure 2.

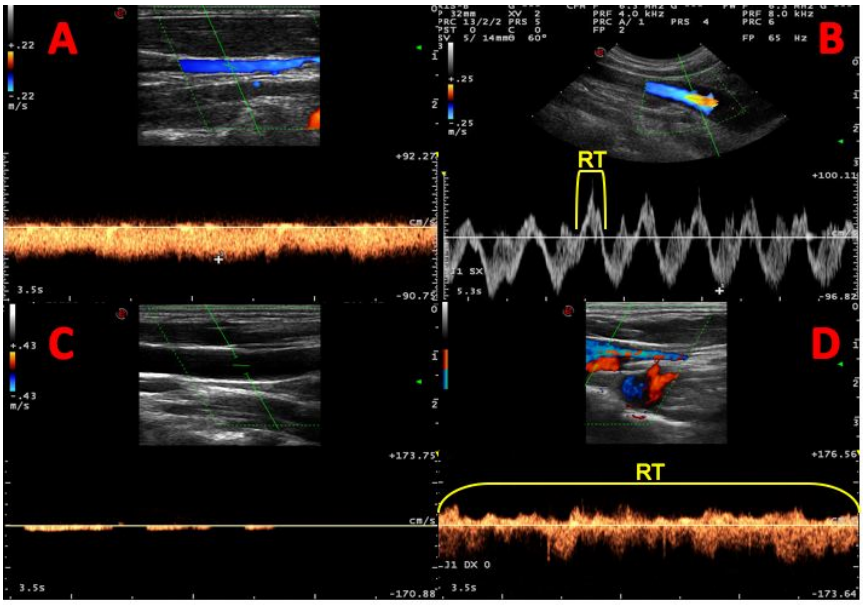

Figure 2. *Upper panels: normal flow traces in the internal jugular vein; lower panels flow traces in CCSVI.*
In A a mono directional flow downward the chest (negative wave) is well apparent, as compared to the flow absence in a CCSVI case depicted in C.
In B the flow in the valvular region is bidirectional for a reflux time (RT) < the cut-off 0.88 sec., whereas in CCSVI case, represented in D, the RT is > of the cut-off (3.5 sec).

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Competing Interest: we have published results that are disputed in the commented article.[1,15]