has ever attempted to show the additional value of CSF markers *over* an MRI investigation – all patients included in the studies, had already undergone MRI or CT (Pijnenburg *et al*., 2006). Having said that, Bouwman and colleagues (2006) have shown that adding CSF to MRI increased the predictive value of both in predicting progression in MCI patients. Again, a clinician will want to see a scan first before applying a lumbar puncture in a routine setting. A frank comparison of the aforementioned two biological markers in the setting of a memory clinic has still to be published (van Gool, 2006).

The same comments apply with regard to functional methods (SPECT and PET). Absence of an indication in primary care seems obvious, but even in the setting of a secondary or tertiary referral center, the added value of SPECT/PET over MRI for the diagnosis of AD is debatable and probably not present (Scheltens *et al*., 1997). Here again, studies have mostly been carried out in selected populations and do not compare the two methods directly. In general, a sensible approach is to limit the application of these methods to cases in which considerable doubt still exists after MRI, usually when MRI is normal. The yield will be highest here in cases of suspected FTLD or DLB (Frisoni *et al*., 2003).

In fact, Professor Wahlund has described what current guidelines already indicate: namely, that structural imaging is required in settings where a nosological diagnosis is needed (Knopman *et al*., 2001; Frisoni *et al*., 2003; Waldemar *et al*., in press) and that MRI is the gold standard in terms of providing both the necessary information to exclude treatable causes as well as the positive information on specific pathology (Scheltens *et al*., 2002). As a note for the future, one may add that the envisioned role of MRI will be to document the extent of underlying pathology(ies) (vascular and degenerative) at the earliest stage possible, even to the extent that clinical labels may eventually become superfluous (Nestor *et al*., 2004; Olde Rikkert *et al*., 2006).

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Commentary: Watson versus Sherlock: Professor Moriarty speaks!

Let us hear what really happened at the Reichenbach Falls near Meiningen, when Dr. Watson (W; performed by L. O. Wahlund, with a sweet Swedish

https://doi.org/10.1017/S1041610206244776 Published online by Cambridge University Press

accent), Sherlock Holmes (S; by P. Scheltens, with only a touch of Dutch) and Professor Moriarty (M; heavy Continental tongue) conversed while out walking:

M: Gentlemen, today, imaging is imperative! But there must have been a time without neuroimaging, when patients had to wait patiently until a grandiose neuropathologist came on his rounds to make an educated guess. That was what one can rightly call suspense – long and deadly! – and an excellent educational experience for junior doctors. Am I right, Watson? What have you learned?

W: *Alzheimer's disease is the most common cause of dementia, followed by vascular dementia, dementia with Lewy bodies and (especially at younger ages) frontotemporal dementia. . . .*

M: This is exactly the kind of traditional botanic view that I despise so much, and which deserves to be abandoned, now that we have learned that there is no dementia in the elderly over the age of 50 without Alzheimer-type neurodegenerative changes!

W: *It is essential that everyone presenting with signs suggestive of cognitive failure is given the opportunity to undergo a full assessment . . . However, it is equally essential that investigations are appropriately targeted, according to their evidence base . . .*

M: I am certainly fond of contradiction and conflict, particularly when they flow so fluently from one person's pen.

W: *. . . evidence base, and only undertaken when they have the potential to have a significant bearing on diagnosis or management.*

M: This is exactly why one should always only choose the winning numbers in a lottery!

W: *A trained clinician with expertise in the differential diagnosis of dementia can diagnose up to 80% of all cases of AD.*

M: A blind man with a stick can get the diagnosis right – if it is Alzheimer's in a psychiatric memory clinic setting or if it is "vascular dementia" in the aftercare of a stroke unit! No CT, MRT or SPECT needed! Remember Reverend Thomas Bayes from Tunbridge Wells.

W: *Other diagnostic criteria for subtypes generally have high specificity (80–90%), but sensitivity may be somewhat lower, around 50% or even less.*

M: How sad! But it is not about detecting other forms of dementia (which do not exist on this planet). It is about identifying additional pathophysiologically relevant facets of dementia, offering additional prophylactic or therapeutic options.

W: *Several new studies indicate that the frequency of secondary treatable conditions is relatively low . . . between 0% and 23%.*

M: Watson, walking around in circular arguments may cause dizziness and great confusion! Why have the reversible forms of dementia become so rare?

https://doi.org/10.1017/S1041610206244776 Published online by Cambridge University Press

Because awareness and differential diagnostic skills and tools have improved! Neuroimaging is certainly the outstanding example of these tools.

W: *Depression and medical side-effects were the most common causes of dementia.*

M: So what, Watson? This statement applies because discerning general practitioners and radiologists had already ruled out the brain tumors, and no longer considered the associated cognitive deficits as signs of dementia! Are these iatrogenic and functional forms of "pseudo-dementia" mentioned to suggest that reversible forms of dementia were generally not so dangerous and important at all?

W: *From both an evidence-based perspective and the perspective of health care economics, one can conclude that there is no evidence to support the view that structural methods (CT and MRI) are of general value within primary care in the context of differential diagnosis of dementia.*

S: *Dr. Watson has made a convincing case that structural imaging is not useful as an adjunct investigation in all cases of dementia in the primary care situation. In my opinion, no one has ever suggested that it would or should be.*

M: Sorry, I am not convinced! Such are the arguments and the intellectual that could make me throw myself down these Reichenbach Falls! And I wish that I could take one of you with me!

S: *Primary care is not the setting in which brain imaging should be performed . . . and it would be overkill, to say the least.*

M & S: Aaaaaaaaaaaaaaaahhhhhhh !!!! [both vanishing with a Doppler-effect]

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Conflicts of interest

John O'Brien has acted as a consultant for G.E. Healthcare.
Hans Förstl has received fees from General Electric, many pharmaceutical companies and many research foundations.

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https://doi.org/10.1017/S1041610206244776 Published online by Cambridge University Press

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