Education

Head turning sign

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Abstract

The head turning sign was first described as such more than 20 years ago but only recently have empirical studies of the sign in large cohorts of patients being assessed for cognitive disorders been reported. Although precise operationalisation of the sign has differed between studies, nevertheless it appears to be frequently observed in cognitive clinic patient cohorts, more so in Alzheimer's disease than in other dementias and with an intermediate frequency in mild cognitive impairment. Head turning is an easily observed and categorised sign and may raise suspicion of the presence of a cognitive disorder. The exact neuropsychological, psychiatric and neurobiological correlates of the sign remain to be determined.

Keywords: Alzheimer's disease, dementia, diagnosis, head turning sign, mild cognitive impairment

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Introduction

The head turning sign (HTS) was previously characterised as a 'noncanonical' neurological sign. This adjective was chosen because HTS did not feature in standard neurological texts at the time.[1,2] This situation is now changing, with head turning referred to in recent texts devoted to both cognitive[3] and general neurology.[4,5] Accordingly, a brief review of the existing evidence would seem to be timely.

History

Based on review of the available literature, it appears that, HTS was first described as such by Bouchard and Rossor in 1996:

> the physician may observe that the patient exhibits the head turning sign (looking at his care-giver when asked a question), which is a common sign in A[lzheimer's] D[isease].[6]

This sign had probably been noted by earlier physicians, for example as a dementia patient's tendency during case taking to refer any questions to the person accompanying them.[7]

Nomenclature

Phenomena consistent with HTS have also been described as 'positive head tilt',[8] but this nomenclature is not advised as it might be confused with the head tilt observed in patients with some forms of diplopia (e.g. fourth cranial nerve palsy) or cervical dystonia.

Head turning has also been used to describe a symptom observed in focal onset epileptic seizures, without apparent lateralising or localising significance.[9]

HTS is entirely different from the 'head turn test' or head tracking test, a computerised measure of complex motor function requiring subjects to follow a moving object by moving their head, previously suggested to be of diagnostic use in Alzheimer's disease (AD).[10]

Operationalisation and quantification

HTS has been operationalised in different ways. This is an important consideration when comparing studies of HTS, although these specifications are of course not obligatory when observing for HTS in day-to-day clinical practice.

Ghadiri-Sani and Larner adjudged HTS to be present (HTS+) if, following introductions and pleasantries (which should permit the identification of any significant hearing impairment which might influence the sign), the patient turned her/his head away from the interlocutor and towards the accompanying person(s) when first invited to describe symptoms (e.g. 'Tell me about the problems you are having with your memory') or when specifically asked about them (e.g. 'What problems are you having with your memory?' or 'Can you give me an example of how your memory lets you down?'). A verbal request for assistance from the patient to the caregiver was not required.[11,12]

Stricter operationalisation has been used in other studies,[13–15] all of which specify that the patient be sat in front of his/her

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Table 1 Head turning sign prevalence in experimental and observational studies

Ref	All	Dem	MCI	No	AD	PSP	VaD	DLB	bvFTD
Experimental studies									
Fukui et al.[13]	–	–	0.25	–	0.42	0.25	0.17	0.15	–
Duraes et al.[15]	–	–	0.50	–	0.79	–	–	–	0.41
Observational studies									
Larner[11] and Ghadiri-Sani and Larner[12]	0.43	0.70	0.57	0.06	–	–	–	–	–
Soysal et al.[14]	0.46	0.88	0.50	0.35	–	–	–	–	–

AD: Alzheimer's disease; All: overall; bvFTD: behavioural variant frontotemporal dementia; Dem: all dementia; DLB: dementia with Lewy bodies; MCI: mild cognitive impairment; No: no cognitive impairment; PSP: progressive supranuclear palsy; Ref: reference number; VaD: vascular dementia

caregiver at an approximate distance of 1 m and at a 45° angle. This point aside, Soysal et al.[14] used similar criteria to Ghadiri-Sani and Larner for HTS, noting head movement in response to questions such as 'What kind of memory problems are you experiencing?' or 'Would you please give a few examples of what you forget?'.

Fukui et al.[13] considered HTS present only when patients turned back to face their caregiver(s) during testing with a cognitive screening instrument, implying difficulties the patient could not deal with and needed to ask the caregiver(s) to help them with, either explicitly or implicitly. When patients turned back only once during cognitive testing a HTS severity score of 1 was assigned, with a score of 2 for twice, and 3 for three times or more. Clearly this approach is not feasible if a caregiver, as a third-party observer, is asked to leave during administration of cognitive screening tests, as suggested by some guidelines.[16] For Ghadiri-Sani and Larner,[11,12] head turning later in the consultation, during administration of cognitive screening instruments, was not deemed HTS+, in part because standard practice in their clinic was for these assessments to be performed in the absence of caregivers.

Duraes et al.[15] attempted to quantitate HTS. In their approach, the patient was asked four questions: (1) 'How is your memory doing?'; (2) 'What is the day of the week?'; (3) 'Where are we now?'; and, (4) 'Can you please tell me the name of the pills you're taking at the moment?'. After each question, the examiner waited for a period of 5 s and observed whether the patient made a head movement towards his/her caregiver (other head movements, such as head tilting while thinking or purposeless head movements, were disregarded). HTS was considered positive if the patient made at least one purposeful movement of the head. HTS was ranked (HTS score) 0–4, according to the number of questions after which the patient exhibited this behaviour.

Prevalence

The prevalence or frequency of HTS will of course vary according to the cohort of patients being examined. Broadly, studies may be divided into those in which patient groups were selected based on their known diagnoses (experimental, case referent, proof-of-concept, Phase I or II studies) and those in which relatively unselected (consecutive) and undiagnosed patient cohorts, typical of day-to-day practice, were examined (observational, pragmatic, Phase III studies).

In experimental studies (Table 1, upper part),[13,15] HTS frequency was highest in AD compared to other diagnoses. Fukui et al.[13] (n = 181) found HTS severity scores were ranked from most to least severe as follows: AD, amnestic mild cognitive impairment (MCI), progressive supranuclear palsy, dementia with Lewy bodies, vascular dementia ($p = 0.014$). Both 'AD-related disease' (i.e. AD and amnestic MCI) and female gender showed a significant and independent contribution to HTS occurrence and also predicted HTS severity scores. Duraes et al.[15] (n = 84) found median HTS score to be higher in AD than MCI or behavioural variant frontotemporal dementia (bvFTD; $p = 0.050$, 0.036, respectively).

In observational studies (Table 1, lower part), Soysal et al.[14] (n = 529) found HTS frequency was highest in dementia compared to MCI and no cognitive impairment, a finding confirmed on reanalysis[17] of the Ghadiri-Sani and Larner data (n = 246)[11,12] (both $p < 0.001$). A separate reanalysis of the Ghadiri-Sani and Larner data according to patient gender showed that the null hypothesis that the proportion of HTS+ patients did not differ significantly by gender was not rejected, although a trend was observed ($\chi^2 = 3.26$, degree of freedom = 1, $0.1 > p > 0.05$).[18] In a separate study, HTS was more frequently observed in patients with cognitive disorders (dementia, MCI, transient amnesias: 19.4%) than in those with functional cognitive disorders (4.2%, $p \approx 0.1$).[19]

Diagnostic utility

Sensitivity and specificity are the most frequently used test measures of diagnostic discrimination, followed by positive predictive values (PPV) and negative predictive values (NPV).

Scheltens stated that HTS is a sensitive sign.[4] What is the evidence for the diagnostic value of HTS (Table 2)?

Soysal et al.[14] found HTS to have high sensitivity for the diagnosis of cognitive impairment, indicating that HTS was reliably present in those with cognitive impairment. In contrast, Ghadiri-Sani and Larner found HTS to have high specificity for the diagnosis of cognitive impairment, indicating that HTS was reliably absent in those without

Table 2 Head turning sign diagnostic accuracy for any cognitive impairment (= dementia + mild cognitive impairment) in observational studies

Reference	Sensitivity	Specificity	PPV	NPV
Larner[11] and Ghadiri-Sani and Larner[12] (n = 246)	0.65	0.95	0.95	0.61
Soysal et al.[14] (n = 529)	0.81	0.65	0.42	0.92

NPV: negative predictive value; PPV: positive predictive value

cognitive impairment.[11,12] Looking at diagnostic accuracy by gender in these latter studies, test sensitivity and specificity were better in females (0.72, 0.98, respectively) than in males (0.58, 0.91, respectively).[18]

Explanations for the differences between the findings of these two groups (high sensitivity and NPV[14] vs high specificity and PPV[17]) are not immediately apparent but might be related to methodology (operationalisation), case mix (e.g. older patient age[14]) or cultural factors in the countries where the studies were performed (respectively Turkey[14,20] and the UK[17]). Patient gender might also be a contributory factor (females = 64.8%[14] vs 50%,[2,18] not 47.2% as stated by Soysal and Isik[20]).

Another, global, measure that has been used to evaluate diagnostic utility of HTS is the 'likelihood to be diagnosed or misdiagnosed' (LDM) metric, the ratio of the number needed to misdiagnose to the number needed to diagnose or predict. For meaningful diagnostic signs or tests LDM should be greater than 1, and ideally >>1.[21] Summing the data from the studies by Ghadiri-Sani and Larner,[11,12] for the diagnosis of any cognitive impairment, HTS had LDM between 2.33 and 2.50, which was better than for other 'noncanonical' signs of cognitive impairment.[21,22]

Neuropsychological correlates

Hodges stated that: "Many patients with significant episodic memory problems display the head turning sign … when asked about past life events they appear vague and say something like 'It was a long time ago' while turning to their spouse to fill in the details".[3]

Fukui et al.[13] reported that scores on a cognitive screening instrument (the Hasegawa Dementia Rating Scale) showed a significant and independent contribution to HTS occurrence and also predicted HTS severity scores. They thought HTS might be the consequence of an imbalance between memory impairment and relatively preserved executive function. However, their cohort did not include patients with bvFTD. HTS has been observed in both behavioural and linguistic presentations of FTD.[11,15]

Soysal et al.[14] reported significantly lower scores on cognitive screening instruments such as the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and clock drawing in HTS+ vs HTS- patients, and also in measures of both instrumental and basic activities of daily living ($p < 0.001$).

Duraes et al.[15] reported significant negative correlation of HTS with scores on MMSE ($r = -0.29$, $p = 0.008$) and MoCA ($r = -0.22$, $p = 0.049$).

In the Ghadiri-Sani and Larner study,[12] 92 out of 113 patients assessed for HTS had also been assessed using the Codex (cognitive disorders examination) decision tree comprising a simple clock drawing test and three-word delayed recall. The proportion of patients scoring in the Codex categories taken to be indicators of dementia was greater for HTS+ (27 out of 43) than for HTS- (18 out of 49) patients ($p < 0.02$; Ghadiri-Sani and Larner, unpublished observations).

Psychiatric correlates

Alpert states that 'Psychogenic factors must certainly be taken into consideration' when assessing HTS.[5] One might perhaps intuit that patients suffering with anxiety and/or depression may defer to a caregiver, perhaps as a component of any associated psychomotor retardation, and manifested as HTS. What is the evidence for psychiatric changes associated with HTS?

Duraes et al.[15] reported significant negative correlation of HTS with the Geriatric Depression Score (GDS; $r = -0.33$, $p = 0.002$). Soysal et al.[14] administered GDS to their patients but did not report any data with respect to HTS status.

Neurobiological correlates

Duraes et al.[15] reported significant positive correlations between HTS and cerebrospinal fluid (CSF) biomarkers of AD, namely the proteins t-tau ($r = 0.32$, $p = 0.003$) and p-tau ($r = 0.28$, $p = 0.009$). CSF levels of Aβ42 showed a tendency for a negative correlation with the HTS, almost reaching statistical significance ($r = –0.21$, $p = 0.052$).

Combination of HTS with other signs

Isik et al.[23] have combined HTS with other signs, namely 'attended with' (i.e. attending the memory clinic with a relative, carer or friend to provide collateral history, as instructed, a probable marker of cognitive impairment, in contrast to the 'attended alone' sign,[1] a probable marker of cognitive normality) and applause signs, in the 'triple test' which they find useful for diagnosis of cognitive impairment.[23,24] In an independent cohort this combination of signs was found to have low frequency (4%) with high specificity and PPV (both 1.00) for diagnosis of cognitive impairment, as anticipated with serial combination of tests.[25]

Conclusions

HTS is an easily observed and categorised sign. Some caution is required in interpretation (e.g. deafness,

psychogenic factors), and reported studies may potentially be unblinded if clinicians observing for HTS are involved in criterion diagnosis. Nevertheless, the existing evidence, though limited, suggests that it may correlate with clinical diagnostic, neuropsychological and neurobiological measures associated with cognitive impairment.

More studies related to the neuropsychological, psychiatric and neurobiological correlates of HTS are required, to see if there is a particular relationship to episodic memory decline, whether HTS is an 'early signal of dementia', and whether there are associated behavioural and psychiatric features. These data will determine whether it might be possible to recommend that HTS be adopted as a standard ('canonical') sign to be actively sought in the assessment of patients with cognitive complaints. Currently, it may be concluded that if HTS is looked for it may provide additional evidence for cognitive impairment when present.

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