



available at www.sciencedirect.com



journal homepage: www.elsevier.com/locate/psyneuen



Thyroid stimulating hormone and prospective memory functioning in old age

Åsa Livner^{a,*}, Åke Wahlin^{a,b}, Lars Bäckman^a

^a *Aging Research Center, Karolinska Institutet, Gävlegatan 16, S-113 30 Stockholm, Sweden*

^b *Department of Psychology, Stockholm University, Stockholm, Sweden*

Received 16 January 2009; received in revised form 19 May 2009; accepted 22 May 2009

KEYWORDS

Prospective memory;
Cognition;
Thyroid hormones;
Subclinical
hyperthyroidism;
Old age;
Non-linear

Summary Alterations of thyroid functioning are common in old age. Even among persons free from thyroid disorders, subclinical variations in thyroid functioning may affect cognitive performance. However, it is unknown whether prospective memory (ProM) is related to thyroid stimulating hormone (TSH) variations. An association could be expected, as changes in the thyroid gland have been linked to alterations in frontal brain regions that play a key role in prospective remembering. Thus, the aim of this study was to examine whether subclinical variations in thyroid functioning affect ProM performance. We studied 103 participants, 75 years and older, who were free from thyroid disorders and had serum levels of TSH and thyroxine (T4) within normal ranges. Interestingly, we found a non-linear association between TSH and ProM performance, where persons with TSH levels above the fourth quartile performed substantially better than persons in the other quartiles. T4 levels were unrelated to ProM performance. This pattern suggests that the previously identified “normal-range” interval for TSH should be moved further up in old age, at least when cognitive functioning is considered.

© 2009 Elsevier Ltd. All rights reserved.

Episodic memory is one of the most aging-sensitive cognitive abilities and critically implicated in many disorders, such as dementia and depression (Bäckman et al., 2001; Tulving, 2002; Nilsson, 2003). When using the term episodic memory, most researchers refer to retrospective memory (RetM), which denotes memory for previously experienced events. However, episodic memory may be decomposed into retrospective and prospective remembering. Prospective memory (ProM) involves remembering to perform an action after a delay (Meacham and Singer, 1977; Ellis, 1996). The action could be carried out either in a specific setting or at a certain time point (Einstein and McDaniel, 1990; Smith, 2008). Two

examples of everyday ProM tasks are remembering to take medication and to make an important phone call. During the last years, the amount of research on ProM has increased. It has also been acknowledged that ProM functioning has important implications for everyday life, and that self-reported ProM failures are common in both clinical settings and in healthy populations (Smith et al., 2000; Kliegel and Martin, 2003). Further, evidence suggests that persons who experience subjective memory problems show deficits in ProM tasks, but not necessarily in RetM tasks (Mäntylä, 2003).

All ProM tasks involve two components: one that is purely prospective and one that is similar to a RetM task (Graf and Utzl, 2001). Whereas the prospective component involves remembering that an action should be carried out, the retrospective component involves remembering what type of

* Corresponding author. Tel.: +46 8 6906880; fax: +46 8 6906889.
E-mail address: asa.livner@ki.se (Å. Livner).

action should be performed. Studies employing functional neuroimaging or event-related potentials have identified several brain regions that are implicated in different aspects of ProM. These regions include frontal areas, the extrastriate cortex, medial-temporal, and parietal areas (West, 2008). Findings suggest that prefrontal regions are essential for remembering the prospective component (Okuda et al., 1998; Kliegel et al., 2008), and the rostral prefrontal cortex appears to play a particularly important role in attentional processes involved in ProM tasks (Burgess et al., 2008). It is also suggested that memory for the retrospective component of the task is largely depending on medial-temporal regions (Kliegel et al., 2008), which is also the case for RetM in general (Squire, 1986; Nyberg and Tulving, 1996; Vargha-Khadem et al., 1997).

Aging is associated with a variety of biological changes, including alterations of the thyroid gland. Manifestations of thyroid abnormalities in old age can sometimes go unnoticed, as the symptoms may be attributed to other disorders or to general effects of aging (Griffin and Solomon, 1986; Biondi and Cooper, 2008). Serum thyroid stimulating hormone (TSH) and thyroxine (T4) levels are indicators of thyroid functioning. Hypothyroidism involves lowered levels of T4, which in turn cause higher levels of TSH through compensatory mechanisms. Correspondingly, hyperthyroidism involves raised T4 levels and low levels of TSH. To distinguish normal from pathological hormone levels is not always a straightforward task; there has been much debate about which cut-offs to use (Biondi and Cooper, 2008).

Both hypo- and hyperthyroidism as well as subclinical states often occur together with psychiatric symptoms (such as anxiety and depressed mood) and impaired cognitive functioning, although the associations are not always clear due to many possible confounding factors (Biondi and Cooper, 2008). It is also suggested that subclinical thyroid disease can increase the risk of dementia (Kalmijn et al., 2000; van Osch et al., 2004). Two previous studies, which, like the present work, were based on data from the population-based Kungsholmen project have addressed thyroid-related cognitive alterations among persons free from thyroid disorders. In one study, persons with lower normal-range levels of TSH performed worse on tests of RetM compared to persons with higher normal-range TSH levels, whereas T4 levels were unrelated to cognitive performance (Wahlin et al., 1998). Interestingly, another study found that lower TSH levels preceded RetM impairment, which supports the idea of a causal association (Wahlin et al., 2005). However, other studies have found no associations between thyroid status and measures of RetM, attention, and cognitive speed (Gussekloo et al., 2004) or global cognitive function (Gussekloo et al., 2004; Roberts et al., 2006).

These studies did not include measures of ProM functioning and, to the best of our knowledge, no study on thyroid function and ProM has been performed. A thyroid-related effect on ProM could be expected, given that previous research has indicated that hyperthyroidism and related states can cause negative changes in many regions of the brain, including the frontal lobes. These alterations include electric activity (Munte et al., 2001), perfusion (Fukui et al., 2001), and metabolism (Bhatara et al., 1998; Fukui et al., 2001) in prefrontal regions.

In light of this background, we sought to examine whether subclinical TSH and T4 variations affect ProM performance. Thus, the main aim of the study was to examine whether alterations in TSH and T4 levels, within normal ranges, affect ProM performance in a group of healthy older adults, sampled from the community.

1. Method

1.1. Participants

The study is based on data from the Kungsholmen project (KP), which is a longitudinal, population-based study focusing on medical, psychological, and social aspects of aging. All inhabitants of the Kungsholmen parish in Stockholm, Sweden who were 75 years or older on 1 October 1987, were included in the original sample ($n = 2368$). The baseline assessment involved two phases: first, 1810 persons participated in a screening phase, which consisted of a health examination and an interview including the Mini-Mental State Examination, or MMSE (Folstein et al., 1975). Second, all participants who scored 23 or lower on the MMSE ($n = 314$) participated in a clinical phase together with a random sample ($n = 354$) of persons who scored 24 or above on the MMSE. These two samples were matched on age and sex distribution. The clinical phase consisted of an extensive medical examination, social interviews, and a comprehensive cognitive test battery. At follow-up examinations, with approximately three-year intervals, all participants were again invited, using the same extensive protocol as in the clinical phase of the baseline examination.

A detailed description of the KP has been reported elsewhere (Fratiglioni et al., 1992), and only a brief description is given here. The KP has been approved by the ethics committee of Karolinska Institutet, Sweden, and informed consent was obtained from all participants or next-of-kin.

The sample used in this study consists of nondemented persons who completed the cognitive testing at the KP baseline assessment ($n = 376$). Dementia diagnoses were made according to DSM-III-R criteria (American Psychiatric Association, 1987). Participants with psychiatric disorders, such as psychosis, major depression, or paranoia ($n = 18$), and persons who did not fulfil the criteria for any psychiatric disorder but were on antipsychotic or antidepressive medication ($n = 17$) were excluded from the sample. For 43 participants, lab data were lacking either because of refusals ($n = 36$) or because the blood vessels were too frail ($n = 7$). Persons with TSH or T4 levels outside previously established cut-offs, indicating thyroid-related or other forms of disorders, were also excluded ($n = 57$). These were persons with TSH levels below 0.4 mU/l or above 5.0 mU/l (Griffin and Solomon, 1986), or free T4 levels below 12 pmol/l or above 25 pmol/l (Retetoff, 1989). Also, we excluded persons who were treated with thyroid hormones ($n = 16$). We also decided to remove participants with serum folic acid levels below 11 nmol/l ($n = 25$) from further analyses, as this is an indicator of folate deficiency, which can be negatively related to episodic memory performance (Wahlin et al., 1996). In addition, we excluded persons in a preclinical stage of dementia (i.e., persons who were dementia-free at baseline, but diagnosed with dementia during the follow-up;

متن کامل مقاله

دریافت فوری ←

ISIArticles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات