Visual-Spatial and Temporal Integration in Patients with Hypothyroidism

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ABSTRACT

Thyroid hormones play an essential role in brain functioning not only during development, but also in adult life. A link between visuospatial abilities and thyroid hormones has already been established. However, it is unclear whether this link is related to the changes in visual information processing, whether the ventral or the dorsal streams are more affected, or the interaction of the two pathways is impaired. The present study aimed to evaluate the effect of hypothyroidism on the visuospatial abilities related to the ventral and dorsal visual pathways using behavioral tasks. Twenty-six newly diagnosed hypothyroid patients and 26 euthyroid controls took part in the study. They had to determine whether the virtual center of radial Glass patterns (GPs) was shifted to the left or right of the screen center, or to discriminate between radial and concentric GPs with varying coherence. Three different conditions were applied: static and two dynamic flicker conditions with a limited lifetime of the dot pairs. The results show that the coherence thresholds were higher in the static condition and the center location task for both groups. The hypothyroid group had higher thresholds in discriminating the radial from the concentric patterns in the dynamic flicker conditions. The proportion of correct responses was lower in the hypothyroid group for patterns with the centers shifted to the right and for concentric compared to the radial patterns. The control group showed decreased performance in localizing the pattern centers shifted to the left. The findings imply that hypothyroidism leads to subtle changes in integrating spatiotemporal information that might be related to deficient processing in the ventral system and the reallocation of spatial attention under cognitive load.

KEYWORDS

hypothyroidism
visual streams
ventral
dorsal
Glass patterns
spatial and temporal processing

INTRODUCTION

Thyroid hormones (TH) such as thyroxine or tetraiodothyronine (T4) and triiodothyronine (T3) have an essential role in normal brain functioning. (e.g., Bernal, 2005; Bernal & Nunez, 1995; Dussault & Ruel, 1987; Rovet, 2014). They have a significant role in brain development, affecting cell migration and differentiation, myelination, and synaptogenesis (Bernal, 2007). In the adult brain, they are involved in regulating energy consumption in processes like neurotransmission, memory, and other higher brain function, and they play an essential role in brain plasticity (e.g., Schroeder & Privalsky, 2014).

Very few studies have examined the effect of thyroid deficiency on perception. These studies typically used specific tests to investigate the effect of hypothyroidism on particular perceptual abilities. Visual deficits such as prolongation of reaction time (Jaiswal et al., 2016; Vedavathi et al., 2013), prolongation of latency, and reduction of the amplitude of visually evoked potentials (Holdew & Condon, 1989; Jaiswal et al. 2016), reduction of the critical fusion frequency of flicker (Dietzel et al., 2012), as well as color deficiencies (Cakir et al. 2015; Racheva et al., 2020) have also been observed in patients with acquired primary hypothyroidism.

Standard neurocognitive tests showed an association between the levels of thyroid hormones and the performance on visuospatial/visuoconstructive tasks (e.g., Beydoun et al. 2015; Correia et al., 2009; Osterweil et al., 1992; Wang et al., 2013). Simic et al. (2013) obtained contradictory results on the role of thyroid hormone deficiency in children and adolescents' visuospatial abilities using two different tasks: line orientation and mental rotation. This study allowed for identifying a common deficit in the hypothyroid group: their inability to integrate parts to form a unified whole.

One hypothesis about the effect of thyroid hormone reduction on visuospatial abilities is that it affects the development of the dorsal and the ventral system differently, that is, the where and what systems (e.g., Leneman et al., 2001). Substantial evidence based on electrophysiological studies in nonhuman primates and neurological

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case studies support the segregation of the visual system into these two streams (Milner & Goodale, 1995). Both streams originate in the primary visual cortex. The ventral stream continues along the ventral surface into the temporal cortex, whereas the dorsal stream continues along the dorsal surface into the parietal cortex. The two streams have different functional properties. The dorsal stream is considered to be involved in spatial processing, motion, and goal-directed actions. The ventral stream is assumed to participate in object recognition and shape discrimination. The two streams are referred to as the where and what pathways to underlie their different connections to action and perception. Recent evidence suggests that the two streams do not work in isolation but interact with each other (e.g., Milner, 2017).

Both the ventral and dorsal streams are involved in visuospatial processing, or the ability that allows a rich and fine-grained understanding of the visual world as the basis for efficient behavioral and cognitive interactions with the environment (Stiles et al., 2020). The role of the ventral stream is related to global-local processing, face perception, and spatial construction, whereas the dorsal stream – to spatial localization, spatial attention, and mental rotation (Stiles et al., 2020). Hence, the ventral and the dorsal stream differ by the visual features they process and by the tasks in which they are predominantly involved.

Using a battery of standard neuropsychological tests related to visuospatial abilities, Leneman et al. (2001) showed impaired processing on the tests related predominantly to the processing in the where pathway that depended on the severity of early hypothyroidism. The standard tests the authors used implied the involvement of the dorsal and ventral streams. However, they could not differentiate the exact time when the two pathways intervened. To shed light on the developmental trajectory of the dorsal and ventral pathways, a later study by Simic and Rovet (2016) testing the effect of thyroid deficiency on visuospatial children's abilities obtained different results about the thyroid hormone effects on the where and what pathways during brain development. The authors used localization and identity tasks with the same stimuli (buildings or faces) to separate the contribution of the dorsal and ventral pathways to task performance. In the first task, the participants were required to compare the position of two sequentially presented photographs, while in the identity task – whether their content was the same. This later study showed more prominent effects of age on the ventral stream abilities and more deficient performance by the children with congenital hypothyroidism on the identity task tapping the ventral processes.

The contradictory results of the two studies underline the importance of task specificity in studying thyroid hormone effects on visuospatial abilities. It may explain the conflicting results from the standard psychometric testing used for evaluating cognitive functions found in studies of the different cognitive functions in hypothyroidism like executive functions, memory, and perception. For example, some studies showed memory deterioration (Baldini et al., 1997; Burmeister et al., 2001; Mishra et al., 2018; Monzani et al., 1993; Pardo Campos et al., 2017). Kazhungil et al.(2015, p. 1) even stated that "memory deficits are the most consistent cognitive dysfunction associated with hypothyroidism." However, other authors claim no changes in memory (Bono et al., 2004), working memory (e.g., Simic et al., 2013; St John et al., 2009), or verbal memory (Kazhungi et al., 2015; Pandey et al., 2017).

A question arises whether some of the controversial results on the thyroid effects on cognitive functions are not related to particular sensory deficits and to the involvement of both the dorsal and ventral systems in the standard neuropsychological battery of tests. It is unclear whether deficits in visuospatial skills in adult hypothyroidism observed on standard neuropsychological tests (e.g., Correia et al., 2009; Wang et al., 2013) are caused by the negative impact of reduced thyroid hormones on visual information processing. It is unclear which steam, the ventral or the dorsal, is more affected or if the interaction of the two pathways is impaired.

In the present study, we aimed to examine the effect of hypothyroidism on the visuospatial abilities associated with the ventral and dorsal visual pathways. For this purpose, we applied specially designed tasks requiring the integration of local spatial information. We used the so-called Glass patterns (GPs, Glass, 1969) that consist of randomly positioned dot pairs (dipoles) whose orientation determines the patterns' global structure. Static GPs require the integration of local orientation of the dipoles in a global form, and hence, their processing is expected to rely mainly on the ventral system. We also used a sequential presentation of the GPs with dipoles of a limited lifetime. This type of stimulation was similar to the so-called dynamic GP produced by the sequential generation of independent static GPs. In processing the dynamic GPs, form and motion information interact (e.g., Donato et al., 2021). The detection thresholds showed similar effects of global shape as in static patterns, implying the involvement of temporal integration of the subsequent frames (Nankoo et al., 2012) and the interaction of the dorsal and ventral streams.

To further separate the contributions of these pathways, we used two tasks. The first one, the center localization task, required distinguishing whether the virtual center of the radial patterns was shifted to the left or the right from the screen center. The second task, the shape discrimination task, required the detection of the global pattern structure: radial or concentric. In both tasks, we varied the signal-to-noise ratio (coherence) of the patterns by changing the number of the dipoles destructing the global pattern structure. Both tasks could be performed based on the information in a single pattern. Hence, the potential interference of memory deficits was significantly reduced.

We hypothesized that the participants with hypothyroidism would perform worse than the control group in the static conditions due to a deficiency in integrating local spatial information into global forms. Also, the differences would be more substantial in the dynamic conditions due to the reduced speed of information processing in this group (Mishra et al., 2018). Moreover, we expected that the differences in the patterns in the two tasks, asymmetrical in the localization task and symmetrical in the shape discrimination, would affect the performance.

The interdot distance of the dipoles in GPs did not change throughout the experiments. Therefore, the local processing of GPs (i.e., dipole orientation detection) was constant. The two tasks differed in demands. The center localization task required dorsal pathway involvement, as this stream is supposed to be involved in spatial vsion and visually guided action (Milner & Goodale, 1995).The second task involved the ventral pathway predominantly, as this pathway is thought

to subserve object recognition and identification. Therefore, comparing the performance of newly-diagnosed hypothyroid patients with euthyroid controls and depending on the task and the stimulus type, we expected to obtain information on the causes of diminished visuospatial abilities due to reduced levels of thyroid hormones. The findings would potentially reveal the role of thyroid hormones on visuospatial processing in the adult brain.

METHODS

Apparatus

The stimuli were presented at the center of a 21 in. CRT calibrated color monitor (Sony GDM-500) with Intel(R) HD Graphics 630 graphic card at a spatial resolution of 1024 × 768 pixels and a frame rate of 60 Hz. The background was grey with a mean luminance of 23 cd/m^2. The observers sat in a dark room at a distance of 57 cm from the screen with a head fixed by a chin rest. The observation was binocular. At this distance, the screen dimensions were 30 × 40 °.

Participants

This cross-sectional study involved 52 female participants between 18 and 54 years old: 26 patients with primary hypothyroidism (M_{age} = 37.2 ± 9.8, range = 18–53) who have not been treated with levothyroxine and 26 controls without thyroid dysfunction (M_{age} = 39.2 ± 8.5, range = 19–54). The upper age limit was chosen not to exceed 55 years to avoid possible visual deficits due to aging. The reason to select only female participants was to avoid gender bias. Only one participant had postoperative hypothyroidism and two were immunologically negative (most likely autoimmune thyroiditis immunologically negative). The rest of the group had autoimmune thyroiditis. The diagnosis of hypothyroidism was established by measuring the thyroid-stimulating hormone (TSH, normal range = 0.3–4 mU/l) and free thyroxine (FT4, normal range = 9–23 pmol/l). Also, antithyroperoxidase (Anti TPO-At), and antithyroglobulin (Anti Tg-At) for both groups were measured. Participants with normal range hormones and serum antibodies were not included in the study as controls. As the results of the control participants were negative, they are not presented. For the hypothyroid group, free triiodothyronine (FT3, normal range = 3.5–7 pmol/l) was measured in addition (see Table 1). The blood serum tests were performed in the same clinical laboratory. In all participants, thyroid ultrasonography was performed by the same physician. Patients with subclinical hypothyroidism defined as normal FT4 and high TSH levels, and patients with overt hypothyroidism defined as low FT4 with high TSH levels, participated in the study.

All participants underwent an ophthalmological examination, including visual acuity, intraocular pressure, and retinoscopy. Information was obtained about each participant's medical history, medications, and hypothyroidism diagnosis. Participants with ophthalmic diseases or taking medicines known to affect vision were not included in the study. Visual acuity abnormalities were corrected with glasses or contact lenses. Participants with diabetes or other endocrinological diseases apart from hypothyroidism were also not included. Glasses that change light intensity or color were not allowed during the experiment.

The Institute of Neurobiology Bioethics Committee approved this study. Prior to the experiments, informed written consent was obtained from all participants. The study was performed in accordance with the tenets of the Declaration of Helsinki.

Stimuli

For the two tasks, the stimulus generation started by randomly positioning fifty dots in a circular aperture with a radius of 450 px. Each of the dots in the initial pattern was paired with another one placed 30 px away (1 ° under experimental viewing conditions). In this way, the stimuli consisted of 100 dots.

TABLE 1.
Characteristics of Hypothyroid and Euthyroid control groups

Parameters	Hypothyroid group	Euthyroid control group	*p**
Number and gender	26 females	26 females	–
Age (years)	37.2 ± 9.8 (18–53)	39.2 ± 8.5 (19–54)	.453
Mean TSH1 (0.3–4 mlU/l)	16.9 ± 19.6	2.3 ± 1.1	.0008
Mean FT42 (9–23 pmol/l)	12.6 ± 3.19	14.9 ± 2.1	.0049
Mean FT33 (3.5–7 pmol/l)	4.8 ± 0.99	–	–
Anti TPO-At4 positive, %	65.4%	–	–
Anti Tg-At5 positive, %	84.6%	–	–

Note. TSH = thyroid-stimulating hormone, FT4 = free thyroxine, FT3 = free triiodothyronine, TPO-At = anti-thyroperoxidase, Tg-At = anti-thyroglobulin
*results of the *t* test for the differences between the groups.

The stimulus occupied a circular area with a diameter of 15 °. The distance between the paired dots (dipoles) was 1.0 °; the dot's diameter was 0.3 °. The pattern density was 0.57 dots/ °^{2}.

The stimuli differed by the dots' initial positions and the spatial relations between the dipoles conveying different global forms. The spatial arrangement of the dipoles determined the coherence (orderliness) of the patterns and their global structure. The dipoles whose orientation was aligned with the simulated global form were considered signal, whereas the dipoles with random orientation were considered noise. The coherence level was determined by the number of the signal dipoles. For both tasks, two different types of stimuli were generated. For the center localization task at 100% coherence, the dipoles formed radial patterns with the virtual center shifted either to the left or right by 120 px, that is, the dipoles were aligned to invisible lines crossing at a point moved away from the stimulus center. The shifted pattern center was 4 °, away from the screen center. Due to the dots' random initial positions and their low density, the exact location of the virtual pattern's center varied slightly.

For the shape discrimination task at 100% coherence, the two types of stimuli were either concentric or radial patterns. In the first case, the dipoles were tangential to invisible concentric circles whereas in the second, they were aligned with virtual lines crossing in the stimulus center. We varied the coherence level by changing the orientation of a different number of dipoles. For each type of stimuli and task, patterns with fifty different coherence levels were generated. The number of noise dipoles increased by one in each subsequent coherence level. There were ten exemplars for each coherence level. Depending on the participant's response, patterns with the proper coherence level were randomly selected from among the existing exemplars. Figure 1 shows examples of patterns with 100% coherence.

We also generated dot patterns for two dynamic conditions that differed with respect to the static condition and the number of frames. In these conditions, one-third of the dot pairs were changed on every frame, keeping the overall coherence level unchanged. Thus, the dot pairs had a lifetime of three frames. The frame duration in one of the dynamic conditions (Flicker 1) was 100 ms, while in the other dynamic condition (Flicker 4) it was 400 ms. The 100 ms frame duration corresponded to the temporal integration of neurons in the early visual areas (e.g., Burr, 1980), whereas the duration of 400 ms was more appropriate for the occurrence of long-range apparent motion (e.g., Braddick, 1980). Usually, the dynamic GPs consist of different stimuli with the same coherence and geometric transformation applied to the dipoles in the stimulus generation. Hence, the sequential patterns are uncorrelated. However, we kept a random portion of the patterns unchanged, similarly to the stimulus generation of random kinematograms with limited lifetime and asynchronous appearance of the dots.

Procedure

A red fixation point was presented at the screen center for 500 ms before each trial. The stimulus presentation included 30 frames with a duration of about 100 ms (for the static condition, the same stimulus was presented on all frames). The total stimulus duration was 3 s. In both tasks, the participants used the mouse buttons to indicate their choice.

All tasks started with 100% coherence. Two intermingled staircases (2 down, 1 up) were used. The staircase order was randomly selected on every trial, but the second staircase started no earlier than the fifth trial with a coherence of 20%. In this way, the first trials could be regarded as practice, as the stimuli could be clearly distinguished. The stimulus type on every trial was randomly selected, whereas the coherence level depended on the response correctness. The coherence level changed by

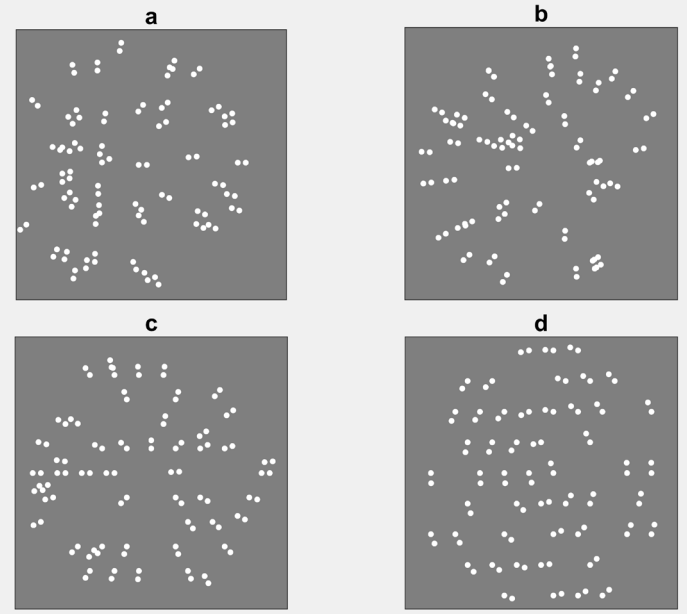

FIGURE 1.
Example stimuli used in the center localization task (Panel A: center shifted to the left. Panel B: center shifted to the right) and in the shape discrimination task (Panel C: radial, Panel B: concentric) with 100% coherence.

one pair of dots. The testing was terminated after 12 reversals or after the presentation of 120 trials.

Each experimental session lasted about 20-30 minutes and contained a single temporal condition (static, Flicker 1, or Flicker 4). The experiments were performed on different days, with intervals depending on the availability of the participants. The order of the experimental sessions and the tasks was counterbalanced across the participants.

Statistical Analyses

All analyses were performed in *R* (R Core Team, 2017). Two types of analyses were performed. The first one was based on the 70.9% thresholds obtained from the averaged stimulus levels of response reversals in the staircase data. The other one was based on the proportion of correct responses received at all presented stimulus levels in the staircase procedure. This analysis relied on having enough repetitions at most stimulus levels permitting to fit a psychometric function. The *lme4* package (Bates et al., 2015) was used to evaluate the effect of the experimental factors on the thresholds of the participants and for fitting a psychophysical function to the proportion of correct responses and the coherence level. A generalized linear mixed model for a binomial distribution and logit link function (the default for binomial family) was used. This choice was based on having binary responses at the stimulus levels used. The count of the correct responses was assumed to be a binomial random variable. The *mafc.logit(2)* function from the *psyphy* package (Knoblauch, 2014) was used to fix the lower asymptote to 0.5 for a two-alternative forced-choice task. The participants were considered a random factor, and group, task, and experimental condition were fixed factors. Models with random slopes and intercepts were tested. We checked the modeling results for overdispersion, homogeneity of the residuals, and outliers using the *DHARMa* package (Hartig, 2019).

The *car* package (Fox & Weisberg, 2019) was used to represent the main effects and interaction terms' significance more compactly as Wald's χ^2 tests (Agresti, 2002).

RESULTS

We analyzed first the thresholds obtained in the two tasks separately. The analysis of variance (ANOVA) results for the influence of the group and the experimental condition showed that in the center location task, the only significant effect was the experimental condition, $\chi^2(2) = 156.65$; $p < .001$. This effect was due to statistically significantly higher thresholds for the static than for the dynamic conditions. The effect of the group, $\chi^2(1) = .04$; $p = .83$, and of the interaction between the group and the conditions was not statistically significant, $\chi^2(2) = 1.08$; $p = .58$.

In the shape discrimination task, both main effects were significant, $\chi^2(2) = 44.49$; $p <. 001$, for the effect of condition and $\chi^2(1) = 4.06$; $p < .05$, for the group effect, whereas the interaction between them was not statistically significant, $\chi^2(2) = 2.18$; $p = .33$. The thresholds for the hypothyroid group were higher than for the control group. There were significant differences between the thresholds for the static condition and the dynamic conditions, with higher thresholds for the static condition. Figure 2 presents the mean thresholds for both tasks and the three experimental conditions.

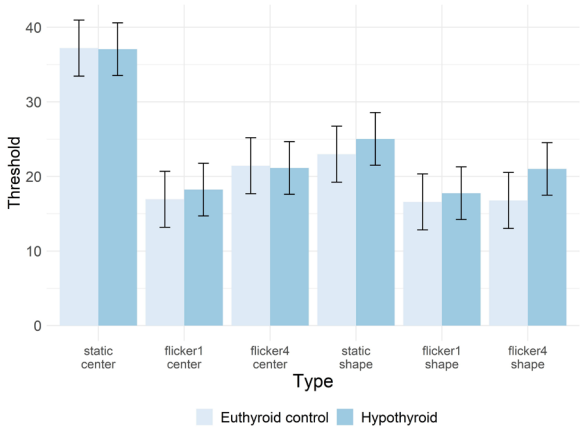

FIGURE 2.

Averaged thresholds for the control and patient groups for the two tasks and the three experimental conditions. The error bars indicate the 95% CIs.

The analyses on the thresholds obtained in both tasks showed a similar effect of the tasks' temporal characteristics, with a mildly inferior performance for the patient group in the shape discrimination task. However, in this task, the performance might have depended on the stimulus type: radial or concentric. In addition to using the thresholds to describe participant performance, we used the raw data and fit a psychometric function of the type:

$$\psi(x) = \gamma + (1-\gamma) * \text{fun}(x) \quad (1)$$

to describe the effect of stimulus coherence on the proportion of correct responses. In Equation 1, $\gamma = 0.5$ characterizes the probability of guessing in a two-alternative forced-choice task, and fun(x) is the logistic function. In this way, all data were used, and some additional comparisons related to the type of stimuli could be made

We wanted to test the following questions:

1. Are there different effects in temporal and spatial integration between the two groups depending on the task?

2. For each task, does the performance differ depending on the type of stimuli?

To answer the first question, we tested the effect of the task, the experimental condition, the coherence level, the group, and their interactions on the proportion of correct responses.

The modeling results showed significant effects of all main factors. For the coherence level, Wald's $\chi^2(1)$ was equal to 214.21 ($p < .001$). The effect of the task, $\chi^2(1) = 10.46$; $p < .001$, was due to the worse performance in the center location task (average proportion correct of 72.51% [70.34–74.71] in the center location task vs. 76.43% [74.29–78.56] in the shape discrimination task). The effect of condition, $\chi^2(2) = 294.19$; $p < .001$, represents the statistically significant difference in the proportion of correct responses between all conditions (63.88% [61.74–66.21] for the static condition, 81.35% [79.25–83.39] for Flicker 1, and 76.70% [74.51–78.88] for Flicker 4). The control group performance exceeded that of the patient group (76.35% [73.24–79.42] cor-

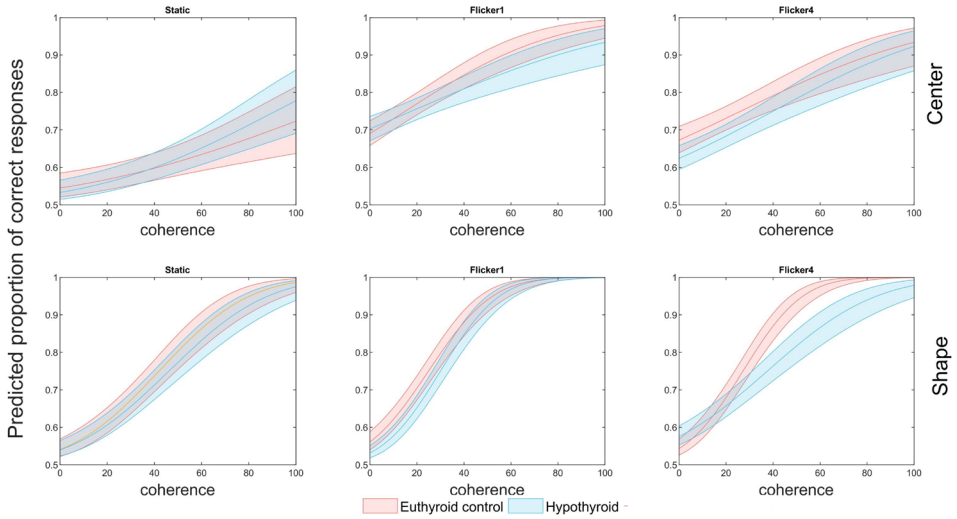

FIGURE 3.

Fitted psychometric functions for the two tasks and in the different experimental conditions with 95% CIs.

rect responses compared to 72.71% [69.98–75.47] for patients; $\chi^2(1) = 4.26$; $p < .05$).

If the performance of the two groups varied differently depending on the task, there should be significant interactions between the group and the other factors. The results showed a nonsignificant interaction between the group and the task, $\chi^2(1) = 1.84$; $p = .18$, implying that the center localization task was more difficult for both groups. However, there was a significant interaction between the experimental condition and the group, $\chi^2(2) = 12.19$; $p < .005$ due to the larger difference between the proportion of correct responses in the dynamic conditions and the static condition for the control group compared to the patient group. The interaction between the group, the condition, and the task was not statistically significant, $\chi^2(2) = .08$; $p = .96$. Hence, the task did not modify the effect of the condition on the task performance of the groups. However, there was a statistically significant interaction between the group, coherence, condition, and task, $\chi^2(2) = 19.23$, $p < .001$.

The fitted psychometric functions and their 95% confidence intervals are presented in Figure 3 for the two tasks and the different experimental conditions. This figure illustrates the interaction between group, condition, task, and coherence level. The figure shows that the two groups differed more in the dynamic conditions, with the most considerable difference in their performance being in the Flicker 4 condition in the shape discrimination task. There was a difference between the two groups in the center location task in the Flicker 1 condition and in the shape discrimination task in the Flicker 4 condition. Moreover, the center location task proved to be more difficult for both groups, as shown by the lower proportion of correct responses, especially in locating the center position in the static condition.

These results show that the experimental conditions statistically significantly affected the performance on the two tasks, and that this influence was not the same for the two groups.

Figure 4 represents the triple interaction between the group, the condition, and the task. It illustrates the similarity in the effects of the dynamic conditions on the participants' ability to discriminate the center positions and the global shapes.

To evaluate the effect of stimulus type on the sensitivity for discriminating pattern' shape or locating the pattern center depending on its position to an implicit reference, we calculated the proportion of correct responses for all participants in a given group for each experimental condition (see Figures 5 and 6). We modeled the effects of stimulus type, coherence level, and group on these proportions. The results showed statistically significant differences between the proportion of correct responses of the two groups for radial stimuli in the Flicker 1 condition, $\chi^2(1) = 5.98$; $p < .05$, the static condition, $\chi^2(1) = 25.32$; $p < .001$, and for all conditions for the concentric stimuli, $\chi^2(1)$

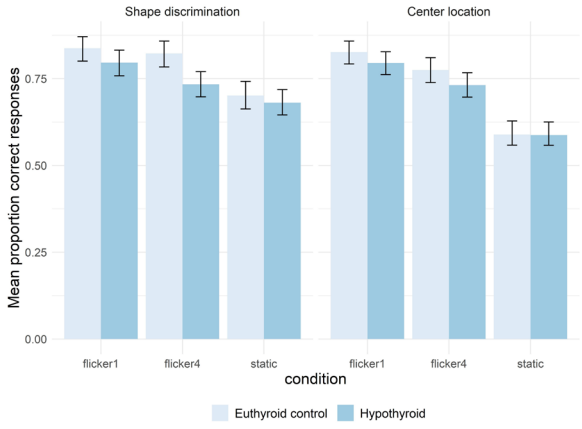

FIGURE 4.

Mean proportion correct for the control and patient groups for the two tasks and the three experimental conditions. The error bars indicate 95% CIs.

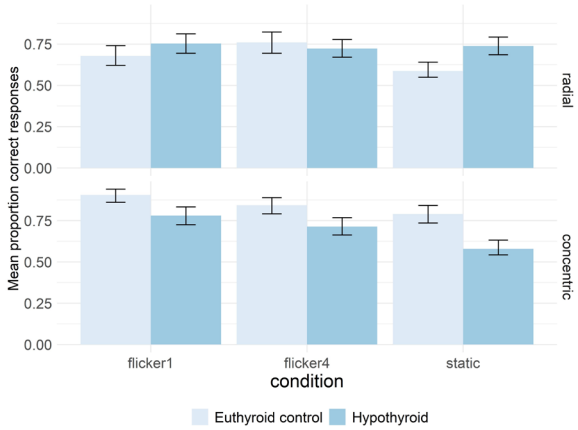

FIGURE 5.

Mean proportion of correct responses for the radial and the concentric patterns for both groups and the three experimental conditions.

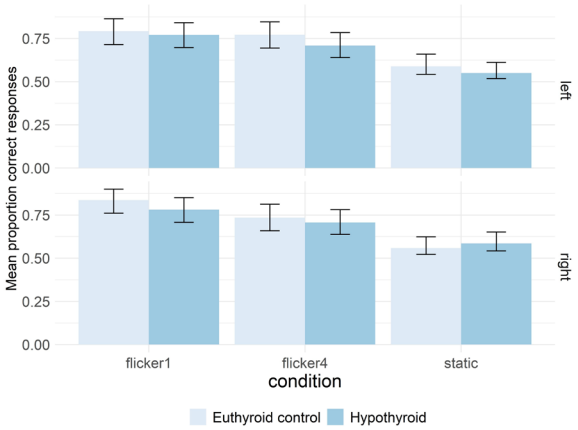

FIGURE 6.

Mean proportion of correct responses for the pattern center shifted to the left and the right for both groups and the three experimental conditions.

= 23.092; $p < .001$, for the Flicker 1, $\chi^2(1) = 7.84$; $p < .001$, for Flicker 4, and $\chi^2(1) = 22.82$; $p < .001$, for the static condition, respectively. For the concentric stimuli, the proportion of correct responses for the control group exceeded that of the patients; for the radial stimuli, the opposite result was obtained.

The results show that in both dynamic conditions with elements of a limited lifetime (Flicker 1 and Flicker 4), performance on the shape discrimination task differed depending on the stimulus type. This finding suggests that the two ex groups have a different sensitivity to the level of added noise, and this sensitivity varies depending on stimulus type. The differences between the two groups are more considerable when the stimuli are concentric than radial patterns.

No statistically significant differences in the percentage of correct responses was observed between the two groups for the center position to the left. However, in dynamic conditions, a statistically significant difference in performance was observed for stimulus center to the right, $\chi2(1) = 11.51$; $p < .001$, for the Flicker 1 condition and $\chi^2(1) = 5.93$; $p < .05$, for the Flicker 4 condition, respectively, with a higher proportion of correct responses for the control than the patient group. Figure 7 shows the fitted psychometric functions for the two tasks in different experimental conditions for the different stimulus types.

DISCUSSION

We aimed to test the hypothesis that hypothyroidism affects the ability to integrate spatial information in untreated patients in tasks involving different ventral and dorsal pathway participation. This hypothesis

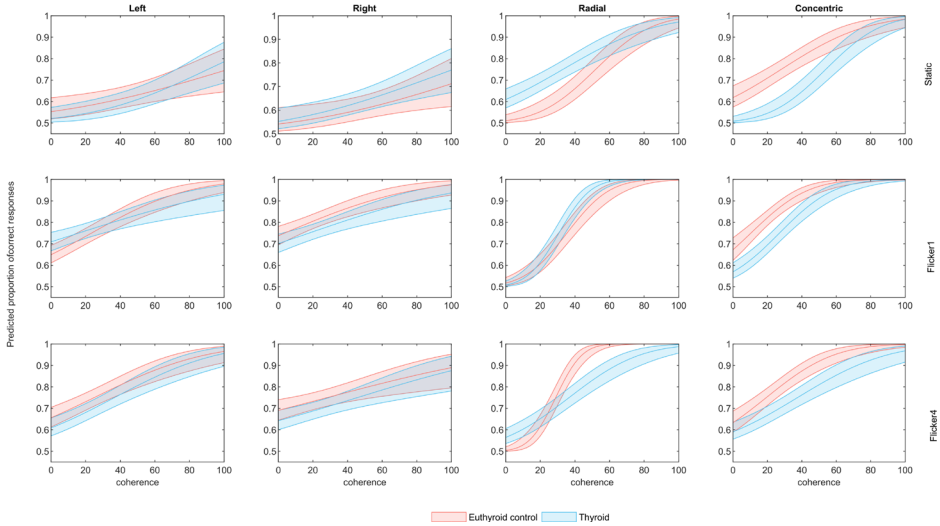

FIGURE 7.

Fitted psychometric functions for the two tasks in the different experimental conditions for the different types of stimuli with 95% CIs.

stems from the existing data (e.g., Leneman et al., 2001) that even after treatment, children and adults with congenital hypothyroidism show mildly deteriorated visuospatial abilities. However, as Simic and Rovet (2016) suggested, this effect might be due to the negative impact of hypothyroidism on the visual system development, more precisely the ventral system. This suggestion implies that hypothyroidism occurring in later years, when visual functions are fully developed, would not affect visuospatial abilities.

However, our data show some differences in performance between euthyroid and hypothyroid groups on tasks requiring spatiotemporal integration, suggesting that the thyroid hormone plays a role in neurotransmission. Thyroid hormones increase the activity of the Na+/K+ATPase and are a potential link to the Na+ current regulation (Dietzel, 2012). To better understand this role, we will consider both the similarities and the differences in group performance.

For both groups, the center location task was more difficult, as evident from the higher coherence thresholds and the lower number of correct responses for this task than for the shape discrimination one. This difference might be due to the stimulus characteristics: asymmetric in the center localization task and symmetric in the shape discrimination task. The visual system is highly sensitive to symmetry. It plays a significant role in perceptual organization. Symmetry can be detected even for very short presentation times (e.g., 25 ms in Carmody et al., 1977, 50 ms in Marković & Gvozdenović, 2001). Symmetrical shapes are detected easier than asymmetric ones (Machilsen et al., 2009). Interestingly, the detection thresholds for symmetry and GPs are similar (van der Helm, 2014). However, global perceptual regularity is perturbed in the radial patterns with a shifted center. Moreover, the localization of the center of the radial pattern required finding the intersection of the virtual lines connecting the dipoles, that is, extrapolating these lines to a common point, a task that might be more difficult at the low dot density of the stimuli.

In both tasks and for both groups, the dynamic conditions improved task performance. It is well known that the detection thresholds for dynamic GPs are lower than for static ones (Burr & Ross, 2006; Donato et al., 2021; Nankoo et al., 2012; Or et al., 2010; Pavan et al., 2017). However, in the dynamic GPs, no correlation exists between the paired dots presented in the sequential frames, that is, on every frame, a newly generated pattern is presented. In contrast, in our study, only one-third of the paired dots changed position. Hence, there was a partial correlation in the positional information of the paired dots in our conditions. As shown by fMRI data, the dynamic GPs invoke activity in the dorsal system similar to real motion, whereas ventral system activation differs depending on the motion type (real or implied; here, we used the terminology of Krekelberg et al., 2005, for the apparent motion occurring in the dynamic GPs). As the dynamic stimuli in our tasks did not induce global motion percepts but apparent local motion (see the Supplemental Materials), one may expect that they did not invoke the same activity in the dorsal system as the dynamic GPs.

The improved performance in the dynamic conditions may be due to the increased number of dipoles during the sequential presentation, and their temporal integration strengthened the signals determining the pattern shape.

We tested the possibility that the participants' performance depends not only on the task but also on the stimulus type. Before, it wass unclear why radial patterns with the center shifted to the left or to the right would be discriminated with different precision. In contrast, the radial and the concentric GPs differ by the curvature of their implied contours, and this difference might affect their discrimination. Our findings showed that the pattern type affected the performance of the two groups differently. The significant main effect of the stimulus type in the center localization task implies that the performance was better when the pattern center was shifted to the left. This asymmetry in performance might be due to spatial attention allocation. Research has shown an asymmetry in visuospatial attention allocation in healthy individuals (young or middle-aged), leading to a leftward spatial bias (Bowers & Heilman, 1980). For example, in the line bisection task, the perceived center is shifted to the left. However, our results showed a significant difference in the proportion of correct responses between the two groups for the center shifted to the right, with better performance for the control group. This result might be due to the control group's better ability to reallocate attention to the right under cognitive load. The experimental evidence shows a rightward shift of visuospatial attention in higher cognitive load conditions (Naert et al., 2018; Pérez et al., 2009). Poorer attention is observed in congenital hypothyroidism (e.g., Rovet & Alvarez, 1996) and adult-onset hypothyroidism (Osterweil et al., 1992). As we had no means to evaluate attention allocation in the present study, this hypothesis is speculative and requires further evidence.

Our results suggest a tendency for local spatial information integration to deteriorate in patients with hypothyroidism in dynamic conditions in both center localization and shape discrimination tasks. This finding might be caused by the reduced speed of information processing in the patient' group (Mishra et al., 2018). A decrease in the conduction velocity can also explain the differences between the two groups. It might increase the correspondence noise between the dipoles in the temporal integration window due to their increased number. Thyroid hormones are essential for the development of glial tissue, and their deficiency can lead to the demyelination of neurons (Bernal & Nunez, 1995; Calzà et al., 2015; Mohácsik et al., 2011; Pinazo-Durán et al., 2011). They are essential for developing oligodendrocytes and for helping their movement in places where there is a lack of myelin (Dugas et al., 2012). Neuron remyelination has been observed in multiple sclerosis with the induction of high doses of thyroxine in rats (Payghani et al., 2018). There are no data in the literature to confirm that hypothyroidism leads to demyelination of neurons in humans, but we can speculate that demyelination is an additional factor for changes in integrating spatiotemporal information in patients with hypothyroidism.

Our results also showed an impaired ability to detect curvature in the patient group. In tasks involving detecting straight contours, as is the case with radial patterns and, to some extent, locating the shifted pattern center position, the two groups' performance was more similar. Previous experimental data showed slightly lower thresholds for de-

tecting concentric than radial patterns (Achtman et al., 2003; Wilson & Wilkinson, 1998) or no statistically significant differences between them in different tasks (e.g., Chung & Khuu, 2014; Lee & Lu, 2010; Schmidtmann et al., 2015). However, in a study by Chen (2009), the author found that circular GPs were significantly easier to perceive than radial GPs. Wilson and Wilkinson (1998) suggested that the spatial integration in concentric GPs was stronger as the neurons in area V4 preferred curved to straight contours. The shape discrimination task in our study could be solved not by discriminating the shape of the GPs but by detecting the presence of either curved or straight contours. The patients' inferior performance for the concentric shapes may indicate a deficiency in visual information processing in the ventral stream.

In sum, our results showed that the euthyroid and hypothyroid groups differed in their performance depending on the type of stimuli, the difference being more considerable in the dynamic conditions. Could there be a common factor that explains the hypothyroid patients' inferior performance compared to the control group in the different experimental conditions? A factor affecting processing speed, attention allocation, and ventral stream processing, related to deficient thyroid hormone? We suggest that it could be the lower dopamine levels in the patient group.

It is well known that dopamine is one of the major neurotransmitters in mediating visual functions in the retina (Brandiesa & Yehuda, 2008; Caravaggioa et al., 2018; Djamgoz et al., 2007; Farshi et al., 2016; Witkovsky, 2004). Low dopamine levels (Dietzel et al., 2012; Ito et al., 1977) and an increase in dopamine receptor concentration and sensitivity (Crocker et al., 1986) were found in hypothyroidism in rats. There is a negative feedback between dopamine secretion and TSH levels (Delitala, 1977). Tyrosine is an aminoacid that is the precursor to both thyroid hormone and dopamine, so high TSH levels and low thyroid hormones can cause low dopamine levels.

Dopamine has an important role in light adaptation and eye growth and affects visual contrast sensitivity, spatial contrast sensitivity, and temporal sensitivity (Djamgoz et al., 2007; Witkovsky, 2004).

Dopamine has complex effects on different cognitive functions. Vitay and Hamker (2008) discussed its impact on visual processing, focusing on its influence on the ventral system's cortical areas, its role on attention and attention shifting, and working memory. Lower performance in the dynamic conditions for the patient group could also be linked to dopamine's effect on the neural signal-to-noise ratio (e.g., Winterer & Weinberger, 2004). The stimulus presentation in the flicker conditions had two effects: it increased the dipole number and created correspondence noise due to apparent motion occurrence between the sequentially presented dots. Yousif et al. (2016) showed that dopaminergic activation could affect perceptual performance by reducing the disruptive effects of increased neuronal noise. Hence, low levels of dopamine may have had adverse effects on the performance in our tasks' dynamic conditions.

In summary, the present results showed subtle differences in spatiotemporal integration of visual information in patients newly diagnosed with hypothyroidism. The observed differences suggest that even when the visual system is fully developed, the TSH deficiency affects the visuospatial abilities and spatial attention in the hypothyroid group. Whether these deficiencies will recover after the inclusion of hormone replacement therapy is the subject of our future study.

Our study involved a relatively small sample over a wide age range. This choice could be regarded as an asset, as the chosen range covers the age of occurrence of hypothyroidism while avoiding the aging effects. However, it also implies increased response variability that might hinder group differences. In future studies, it might be advantageous to increase the sample or restrict the participants' age.

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The authors report no conflicts of interest.

DATA AVAILABILITY

The data are available from the authors upon request. The Supplemental Materials are available at https://osf.io/87buj/

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