THYROID HORMONE AND AFFECTIVE DISORDERS

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Abstract

Thyroid hormones are necessary to the brain development and their absence results into serious cognitive defects. There is some evidence that thyroid hormones' activity is required in the adult brain for a correct neuronal net orchestration as well. The bonds between mood disorders and thyroid imbalances are reviewed in this paper, the molecular background of these poorly defined boundaries is exposed, along with the putative mechanisms that underlie the antidepressant effect of thyroid hormones in the event of augmentation strategy.

Key Words: thyroid hormones, cognitive defects, mood disorders

Declaration of interest: None

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Thyroid hormone

Thyroid hormones – Thyroxine (T4) and Triiodothyronine (T3) – are considered to be essential for cellular metabolism, growth and differentiation of several organs and especially the brain (Bernal 2002, Palha and Goodman 2006, Yen 2001). Thyroxine (T4), which is the major product secreted by the thyroid gland, requires the active uptake of dietary iodine by the gland to be synthesized. Thyroid hormone secretion is tightly regulated by the hypothalamic – pituitary - thyroid axis. The pituitary thyroid-stimulating hormone (TSH) and the hypothalamic thyrotropin-releasing hormone are the major products of the axis that tightly regulate the thyroid hormone secretion. In the circulation, T4 is mainly bound to plasma proteins, namely thyroxine-binding globulin, transthyretin (TTR), albumin and lipoproteins (Palha 2002). Triiodothyronine (T3) is the biologically most active thyroid hormone due to its ability to bind thyroid hormones (TH) receptors with 10-fold higher affinity than T4. T3 derives from T4 through deiodination (Bianco et al. 2002, Palha and Goodman 2006). In the periphery, type I deiodinase in the kidney and liver is responsible for producing most of the circulating T3 whereas in the brain, T3 is produced for local use by the action of deiodinase type II (Palha and Goodman 2006). It is important to be mentioned that deiodinases type I and II are differentially regulated in order to protect the brain from T3 excess or deficiency. In hypothyroidism, the type I deiodinase is down-regulated while the type II is up-regulated; while the opposite regulation occurs in hyperthyroid conditions. Furthermore, inactivation of thyroid hormone is mainly carried out by the action of type III deiodinase (D3), glucoronosyltransferase and sulfotransferases (Leonard and Koehrle 2000). Most thyroid-hormone-mediated actions are controlled by transcriptional regulation (Bassett et al. 2003, Yen 2001). T3 interacts with thyroid hormone receptors (THR) that function as ligand-activated transcription factors. There have been recognized two genes that encode THRs, the THRá and THRâ, which belong to the nuclear hormone receptor superfamily which includes vitamin D (a steroid), retinoic acid, peroxisomal proliferator, and 'orphan' receptors that do not have known endogenous ligands (McKenna et al. 1999), and for each there are splicing variants with distinct developmental roles and tissue distribution patterns (Bassett et al. 2003, Yen 2001). Within the nucleus, THRs recognize hormone response elements in target genes. For activity, however, they need to heterodimerize.

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Thyroid hormones and mood disorder

It is well demonstrated that thyroid hormone receptors are widely distributed in the brain (Carlson et al. 1996; Hwang et al. 2008; Leonard et al. 1994; Wang et al. 1995, 2003), but they are prevalent in the limbic system of the brain, and they have been implicated in the pathogenesis of mood disorders (Bauer et al. 2008): consistently, it has been reported that the glucose metabolism is down-regulated in the limbic system (uncus and inferior temporal gyrus) under condition of tyreotossicosis, whilst activation in the posterior cingulate and inferior parietal lobe are correlated with anxiety and depressive symptoms under the same metabolic condition (Schreckenberger et al. 2006). On the other hand, glucose turn over and blood flow were found to be both decreased in the whole brain in the case of decreased level of thyroid hormones (Constant et al. 2001), and, quite interestingly, a more discrete localization of the diminished blood flow at the parietal lobe and at part of the occipital lobe was described in hypothyroidism after thyroidectomy as well (Nagamachi et al. 2004, Schraml et al. 2006). Further on, it was reported that regions of the brain relevant to attention, motor speed, memory and visuo-spatial processing (namely: lower right parieto-occipital gyri, cuneus, posterior cingulate, lingual gyrus, fusiform cortex, insula and pre and post central gyri), are characterized by a diminished blood flow in patients suffering from Hashimoto's thyroiditis compared to normal controls (Krausz et al. 2004). Even though these results still do not compose a consistent path, there is enough evidence from functional neuro-imaging studies addressing the relevance of thyroid hormones in the brain activity to sustain research toward this direction. Intriguingly, there is some evidence that thyroid hormones activity also results into a neuronal cytoprotective activity: an increased oxidative metabolism was reported in the frontal lobe in hypothyroid patients which was normalized following T4 treatment (Smith and Ain 1995). This line of evidence opens the neuroprotective theory of mood disorders (Pae et al. 2008) to the impact of the thyroid hormones' orchestration, and functionally interlaces it with the known relevance of thyroid hormones in modulating the expression of neurotrophins (Alvarez-Dolado et al. 1994, Neveu and Arenas 1996) as far as neuroresilience and neruoprotection seem to be both impacted by thyroid hormones. However, the cellular and molecular mechanisms underlying these metabolic effects, and the specific neuropharmacological basis and functional pathways for the modulatory effects of thyroid hormones on mood, are yet to be completely understood: some cues are retrieved from the investigation of the monoaminergic systems. Norepinephrine and serotonin , which are believed to play a major role in the regulation of mood and behavior, interact with the thyroid system and may contribute to the mechanism of action in the developing and mature brain (Bauer et al. 2002b, Gordon et al. 1999, Marwaha and Prasad 1981, Whybrow and Prange 1981). Consistently, there is evidence, mainly from animal studies, that the modulatory effects of thyroid hormones on the serotonin system may be due to an increase in serotonergic neurotransmission, and that occurs through a reduction of the sensitivity of 5-HT1A autoreceptors in the raphe nuclei and an increase in 5-HT2 receptor sensitivity (Bauer et al. 2008, Bauer et al. 2002b). Other neurotransmitter systems also involved in mood regulation and interact with thyroid system, including dopamine post-receptorand signal transducing processes, as well as gene regulatory mechanisms (Bauer et al. 2002b, Henley and Koehnle 1997, Mano et al. 1998). For example, the neurogranin (RC3) has been demonstrated to play a pivotal role in synaptic plasticity and learning (Chen et al. 1997), and its expression is enhanced by the presence of thyroid hormones also in adult animal models (Iniguez et al. 1996), especially in the striatum and hippocampus, by the ways of a thyroid hormone responsive element located in its genetic frame (Martinez de Arrieta et al. 1999, Wilcoxon et al. 2007). The striatum is the most relevant source of cerebral inputs of the basal ganglia system, and, quite interestingly, the dorsal part of it is thought to play a pivotal role in regulating the cognitive activities, whilst the ventral part is likely more involved in the regulation of the motor aspects of behavior (Alcaro et al. 2007). The hippocampus is embedded in the limbic system of the brain and provides the neuronal structures responsible for the storing of spatial learning and memories by the long term potentiation effect which is facilitated after the activation of the emotional content resulting from the interplay between the amygdala and the associative areas of the cerebral cortices (Alcaro et al. 2007). By regulating the neuronal plasticity through the activity of the RC3, thyroid hormones may then facilitate the neuronal interplay in this relevant brain region: this provides some more hints to the explanation of some links between hypothyroidism and a poor plasticity in cognitive tasks (Zhu et al. 2006). The molecular path which is associated with RC3 activity encompasses the calmodulin and Ca++ balance and finally results into the enhanced activity of the calmodulin kinase II, an enzyme implicated in synaptic plasticity as well (Miyamoto 2006). Moreover, the Ras pathway which modulates the dopamine system and is involved in neuronal plasticity, was found to be impacted by the thyroid hormones replacement in an animal model of hypothyroidism: in some details, it has been reported that the replacement of T3 led to the modulation of the before mentioned set of key striatal plasticity indicators (neurogranin (RC3), Ras homolog enriched in striatum (Rhes), Ca2+/calmodulin-dependent protein kinase (CaMKII), and dopamine- and cAMPregulated phosphoprotein (DARPP-32)). In particular, the T3 treatment led to the up-regulation of the CaMKII levels and to a decrease of the DARPP-32 phosphorylation (Vallortigara et al. 2008). The DARPP-32 is a relevant signal mediator within the cell whose deregulation has been claimed to be central in psychiatric disorders (Lindskog 2008). Interestingly, it is under the control of dopamine, serotonin, glutamate and adenosine systems: in particular, phosphorylating this this protein at Thr(34) results into a potent inhibition of the multifunctional serine/threonine protein phosphatase PP-1, whilst phosphorylation at Thr(75) converts the DARPP-32 into an inhibitor of the protein kinase A (PKA). Controlling the state of activation of PKA and PP-1 makes the DARPP-32 a regulator of a wide fan of biochemical activities within the neuronal

nets which may result into the molecular disruptions which underlie psychiatric disorders. Including the thyroid hormones within the number of regulators of DARPP-32 further enriches our knowledge on how hypothyroidism and subclinical hypothyroidism may result into a higher risk to experience psychiatric sufferance.

Further on, an intriguing experiment on animal models recently demonstrated that the binding rate of benzodiazepine and opioid receptors was found to be reduced in hypothyroid animals compared to euthyroid ones. Intriguingly, the neuronal sites that were much responsible for this difference were the basolateral amygdala – which conveys the salience of memories and events – the sensorimotor and temporal cortices – which are associated with the associative functions of the brain - along with the ventro posterior thalamic nucleus – a central site for the sensory information flow - (Ortiz-Butron et al. 2003). This finding replicates previous observations that reported on the sensitiviness of mu receptors to thyroid levels in the median eminence – a part of the hypothalamus that connects with the anterior lobe of the pituitary gland – and in the striatum (Bhargava et al. 1989, Calza et al. 1992). Consistently, it has been demonstrated that hypothyroidism induces the up-regulation of some endogenous opioids mRNA (enkephalin and dynorphin) in the limbic system (Giardino et al. 1995). The possible impact of an thyroid driven poor orchestration of the endogenous opiods system over the depressive phenotype may represent the molecular basis of a fan of symptoms ranging from anhedonia to decrease interest for everyday activities.

Interestingly, it has been proposed that a reduced BDZ binding density in the amygdala could be associated with memory alterations (Ortiz-Butron et al. 2003) which could result into the cognitive impairment which is characteristic of depressive states (i.e. recall bias, interpretation bias and so on (Merens et al. 2007)). Finally, there is supportive evidence that thyroid hormones act as modulators of neuroresilience through diverse paths: first, they are able to induce an enhanced glutamate reuptake activity of astrocytes which result into a diminished risk of a glutamate induced neurotoxicity (Mendes-de-Aguiar et al. 2008); second, it has been reported that the expression of a neuroprotective protein referred to as seladin-1 – whose deregulation is associated with Alzheimer's disease – is under the influence of thyroid hormones. Seladin-1 probably acts by inhibiting the activation of the caspase pathway. Nevertheless, within the CNS, the regulatory cascade through which the thyroid hormones, particularly T3, exert their effects is not completely understood: deiodinase activity, nuclear binding to genetic loci and, ultimately, protein synthesis may all be involved and a detailed biological overview on this mechanisms is still lacking which may bridge the suggestive evidence that disturbances or reactive hyperactivity in the HPT axis, as manifested in the blunted TSH response to TRH found in some patients with depression may underlie part of the pathophysiology of mood disorders (Bauer and Whybrow 1990, Baumgartner et al. 1994, Gyulai et al. 2003, Jackson 1998).

Neuropsychiatric changes in thyroid disorders

Thyroid metabolism plays a crucial role in the mature brain and its normal function and any disturbances may profoundly alter mental function, influencing cognition and emotion (Bauer et al. 2008). The most frequently occurring thyroid diseases of adult life are autoimmune disorders, with autoimmune (Hashimoto's) thyroiditis being the most frequent cause of hypothyroidism (inadequate hormone production), and Graves disease being the most frequent cause of hyperthyroidism (excess hormone production). Changes in mood and intellectual performance are closely associated with both hyperthyroidism and hypothyroidism; and severe hypothyroidism can mimic melancholic depression and dementia. It was demonstrated that the neurocognitive impairments accompanying dysfunction of the thyroid gland are usually reversed rapidly following return to euthyroid hormone status, although severe hypothyroidism, if left untreated, may rarely result in irreversible dementia (Bauer et al. 2008, Davis and Tremont 2007, Haupt and Kurz 1993).

Cognitive changes relating to thyroid disease

It was demonstrated that in some patients with hyperthyroidism frequently cognitive symptoms even persist beyond the acute phase (Stern et al. 1996). On the other hand, impairments of cognitive symptoms in patients with hyperthyroidism have only been found inconsistently (Stern et al. 1996). However, cognitive changes have frequently been detected in patients with hypothyroidism, including defects ranging from minimal to severe in general intelligence, psychomotor speed, visual–spatial skills and memory (Burmeister et al. 2001, Dugbartey 1998, Osterweil et al. 1992). Furthermore, in several recent studies demonstrated that the defects of memory in hypothyroid patients are not attributable to an attentional deficit but rather to specific retrieval deficits (Burmeister et al. 2001, Miller et al. 2007). This is consistent with the molecular and neuronanatomical alterations that have been discussed above: a condition of even mild hypothyroidism is associated with the deregulation of the expression patterns of opioid, gabaergic and serotonergic receptors. Moreover, relevant second messengers such as the DARPP-32 have been found to be influenced by the thyroid hormones levels in their activity. Intriguingly, the limbic system is one of the most frequent brain structure that have been associated with these metabolic deregulations. Limbic system is involved in the storing and re-emerging of memories, along with the impression of the emotional value to the events that are both faced at the moment and recalled at memories (Alcaro et al. 2007). Moreover, the involvement of the associative cortices and of the striatum suggests that the cognitive impairment which characterize depressive disorders may be consistently linked to the deficient activity of thyroid hormones. This findings are consistent with the observation that hypothyroidism appeared to have less affect on motor skills, language, inhibitory efficiency, and sustained attention (Burmeister et al. 2001, Dugbartey 1998, Osterweil et

al. 1992). It must be reported that the memory deficit found in patients with hypothyroidism appears to be different from that experienced from patients with major depression, in which patients typically experience broad executive difficulties (Burmeister et al. 2001): this suggests that depressive disorder is fairly more complex in its eziopathology than what could be explained from the imbalance of a single hormonal system. However, older adults suffering from thyroid failure may show an impressive problem of cognitive changes (Davis et al. 2003), which suggests that this specific aspect of depressive disorder is biologically related – even if likely not entirely explicated – by the thyroid hormones' activity. Some interesting cues are related to the subclinical hypothyroidism which is characterized by a serum TSH level elevated above the statistically defined upper limit of the reference range, in association with a serum free T4 level within the reference range (Ross 2001). Recent studies could not demonstrate a definitive association between subclinical hypothyroidism and measures of cognition (Gussekloo et al. 2004, Jorde et al. 2006), whereas, in some other studies, patients with subclinical hypothyroidism performed worse than normal controls on neuropsychological tests (Bauer et al. 2008, del Ser Quijano et al. 2000) or experienced an impaired memory function (Baldini et al. 1997). Of note, elderly patients are reported to be at risk of cognitive impairment, mood disorders, lipid dysmetabolism and cardiovascular abnormalities even in the case of subclinical hypothyroidism (Valenti and Fabbo 1996), showing a pattern of pathological risk that is closed to the hypothyroidism in the adult. It must be reported that with regard to the mood state and cognitive impairment, there is a consistent set of evidence that discourage the hypothesis of a link between mood and cognitive functions with subclinical hypothyroidism (Bell et al. 2007, Gussekloo et al. 2004, Jorde et al. 2006, Roberts et al. 2006). Nevertheless, these negative findings could be related to a not sufficiently sharpened analysis of the cognitive activity: a functional magnetic resonance imaging (fMRI) study found that working memory was impaired in patients with subclinical hypothyroidism, and these impairments were reversible with L-thyroxine (L-T4) treatment (Zhu et al. 2006). There is also argument as to whether the cognitive and mood symptoms of thyroid disease, particularly hypothyroidism, are completely reversible with normalisation of thyroid levels with L-thyroxine. A study comprising 37 000 individuals could not demonstrate any relation between depression and anxiety and thyroid disease (Patten et al. 2006). The significance of this result may be dampened by the fact that thyroid disease was assessed on the basis of a self reported scale, thus exposing the study to a relevant recall bias: mild hypothyroidisms or not treated hypothyroidism may not have been included in the analysis. Moreover, social phobia was found to be actually associated with an history of thyroid disease after correction for relevant covariates such as age, gender, and the presence of other chronic conditions. In another study comprising 30 000 individuals, depression and anxiety were not associated with current thyroid dysfunction, but were associated with prior thyroid disease (Engum et al. 2002). Furthermore, in another study of 165 000 patients with hypothyroidism, there was an increased risk of depression or bipolar disorder especially within the first year of the thyroid dysfunction (Thomsen et al. 2005). Some other studies suggested persistent psychological impairment in a subset of thyroid patients (Samuels et al. 2007, Saravanan et al. 2002, Wekking et al. 2005). Although all the cognitive symptoms of the thyroid patients may be due to inadequate replacement therapy, there is no relationship between current TSH concentration and symptoms (Samuels et al. 2007, Walsh et al. 2006), although this issue remains controversial (Saravanan et al. 2006). It was evidenced through studies on postnatal women and women with Hashimoto's encephalopathy that autoimmunity in thyroid gland may be an independent risk factor for depression or cognitive impairment (Chong et al. 2003, Harris et al. 2002, Kuijpens et al. 2001).

Neuropsychiatric symptomatology in thyroid disease

In case of hyperthyroidism or thyrotoxicosis the patient is characterized by psychiatric symptoms such as dysphoria, anxiety, restlessness, emotional liability, and impaired concentration (Bauer et al. 2008). In elderly patients, depressive symptoms such as apathy, lethargy, pseudodementia and depressed mood can also occur (Bauer et al. 2008). In previous studies it was found that almost 60% of thyrotoxic patients demonstrate an anxiety disorder and between 31% and 69% have a depressive disorder (Kathol and Delahunt 1986, Trzepacz et al. 1988). However, clear psychiatric characteristics occur in approximately 10% of thyrotoxic patients (Bauer et al. 2008). Furthermore, thyrotoxic patients develop mania when there is an underlying mood disorder or positive family history (Hasan and Mooney 1981). This line of evidence further stresses the polygenetic nature of mood disorders. On the other hand, hypothyroid patients, show depression-like symptoms including psychomotor retardation, decreased appetite, fatigue, and lethargy. Neurocognitive dysfunction and depression as well as impaired perception with paranoia and visual hallucinations may develop, and severe hypothyroidism mimics melancholic depression and dementia (Bauer et al. 2008).

Thyroid status in patients with mood disorders

Patients with mood disorders were evidenced that suffer with abnormalities in thyroid hormone metabolism (Bauer et al. 2008). There is no clear sign of thyroid disease in patients with depression although in approximately 15% of the patients subclinical hypothyroidism was diagnosed (Gordon et al. 1999). The recurrence of episodes in depressive patients was found to be inversely correlated to serum T3 but not T4 levels (Joffe and Marriott 2000). In approximately 25-30% of depressed patients, an abnormal TSH response to TRH stimulation is found (Loosen 1985). Elevated T4 level in serum of depressed patients was found to be the biological marker most sensitive to antidepressant treatment (Whybrow et al. 1972), including anti-

depressants, carbamazepine and lithium (Baumgartner and Campos-Barros 1993, Baumgartner et al. 1988, Baumgartner et al. 1996), and after response to nonpharmacological treatments, including sleep deprivation, light therapy (Baumgartner et al. 1996), electroconvulsive therapy and psychotherapy (Joffe et al. 1996).

In general, little is known about the exact interactions between antidepressants and the thyroid hormone system. Interestingly, treatment with antidepressants (desipramine, paroxetine, venlafaxine, tianeptine) in the rat results in a rather specific increase of T3 in the myelin fraction of homogenates of the amygdala (Pinna et al. 2003). A study reported lower levels of CSF transthyretin in depressed patients when compared to healthy controls (Sullivan et al. 1999), suggesting a limitation in the uptake of T4 into the brain via transthyretin, which is synthesized in the choroid plexus. However, in a transthyretin null mice strain, the complete absence of transthyretin has no impact on thyroid hormone levels, development, or fertility (Palha et al. 1994). These findings emphasise the importance of other membrane carrier systems such as MCT8 or OATPs to maintain thyroid hormone homeostasis in the brain (Schreiber 2002). There is also growing evidence of thyroid abnormalities in patients with bipolar disorder. Patients receiving lithium prophylaxis who have free T4 levels in the low–normal range may experience more affective episodes (Frye et al. 1999). Although within the normal range, a lower free thyroxine index and higher TSH were significantly associated with a poorer treatment response during the acute depressed phase of bipolar disorder (Cole et al. 2002). TPO (thyroid peroxidase) antibodies were reported to be elevated in bipolar disorder with a prevalence of 28% (Kupka et al. 2002), whereas results from other studies were inconsistent with reported rates in the range 0–43% (Haggerty et al. 1990, Haggerty et al. 1997, Hornig et al. 1999, Oomen et al. 1996). In community studies, the rates of prevalence of TPO antibodies generally range from approximately 12–18% (Hoogendoorn et al. 2006, O'Leary et al. 2006, Pedersen et al. 2003). The estimate of TPO antibody prevalence will vary with the sensitivity and specificity of the testing methodology (Baloch et al. 2003), is increased in females, in old age (O'Leary et al. 2006, Pedersen et al. 2003), when TSH levels are abnormally high or low (Bjoro et al. 2000, Spencer et al. 2007), and when individuals with known thyroid disease are included in the population. Thyroid antibody status was also associated with an increased risk for lithium-induced hypothyroidism, but not with current or former lithium treatment (Kupka et al. 2002).

Thyroid hormones in the treatment of mood disorders

For the treatment of mood disorders, there has long been an interest in using thyroid hormones because of the relationship between thyroid disease states and psychiatric symptoms. Thyroid hormone monotherapy is not an adequate treatment for patients with primary mood disorders, whilst a series of clinical trials have confirmed the therapeutic value of adjunctive treatment with thyroid hormones in mood disorders (Prange et al. 1969). It was demonstrated that the use of T3 can accelerate the therapeutic response to tricyclic antidepressants (Altshuler et al. 2001).

Moreover, the T3 can be useful in the treatment of resistant depression (Aronson et al. 1996, Cooper-Kazaz et al. 2007). T3 has also been shown to augment the response to sertraline (Appelhof et al. 2004) but not to paroxetine (Bauer et al. 2001). Inconsistently with this, reboxetine was found to be associated with increased THS and decreased T4 levels after effective antidepressant treatment, whilst opposite findings were associated with paroxetine (Eker et al. 2008). These clinical findings are consistent with results reported in animal models and stress the relevance of the thyroid balance during the molecular phases that are associated with the antidepressant treatment. Interestingly, the opposite effect that was detected between reboxetine and paroxetine does not account for the similar antidepressant effect the two molecules have. This apparent conflicting finding further stresses the existence of a complicated neuronal path that underlies depressive phenotype; moreover, it likely suggests that thyroid hormones are implicated in the molecular disruptions that lead to depressive mood, but are not in a linear cause-effect relationship with it.

A molecular model which may underlie the antidepressant effect of thyroid hormones when used with antidepressants has been proposed to be the neuronal bioenergetic balance: Iosifescu and colleagues recently demonstrated that the biological hallmark able to distinguish between responders vs non responders to thyroid augmentation treatment was the enhanced concentration of nucleoside triphosphate in the group of responders (Iosifescu et al. 2008), thus demonstrating that the energy storage within cells may distinguish an effective antidepressant molecular effect vs lack of effect. This is quite interesting and may offer an intriguing explanation of the antidepressant effect of thyroid hormones during augmentation strategy. Consistently, supraphysiological doses of L-T4 showed in a series of studies to be effective treatment for patients with severe rapid cycling or resistant bipolar disorder (Bauer et al. 2002a, 2001; Stancer and Persad 1982) and immediate therapeutic value in antidepressant resistant bipolar and unipolar depressed patients during a phase of refractory depression (Bauer et al. 1998, Rudas et al. 1999). Supraphysiological T4 doses are tolerated surprisingly well without causing any problems of thyrotoxicosis and serious effects even in patients treated for extended periods (Bauer et al. 2004, Cooper-Kazaz et al. 2007, Gyulai et al. 1997). The low incidence of adverse effects and high tolerability reported by patients with affective disorders who are receiving high-dose thyroid hormone therapy contrasts with that typically seen in patients with primary thyroid disease. This may suggest that the thyroid supplementation may support a nervous deserving system in depressed or bipolar patients, in the absence of a clearly diminished blood circulating thyroid hormone levels.

Corollary in clinical practice

Requesting thyroid hormones levels in depressed

patients at first visit in psychiatric bureau is standard procedure. Accordingly, every other possible medical cause of depressed mood, or altered mood as well, should be excluded before a drug treatment with antidepressants or mood stabilizers is begun. The main result of this review is that also a marginal deflection of thyroid hormones levels should attract the attention of a psychiatrist in his everyday practice. In all facts, lower even if still in range thyroid hormones levels may concur to form the intricate biological profile that exposes patients to the risk of experiencing a mood disorder episode, and should be treated accordingly. Thus, it would be worth fixing also the small deviations from the so called normal range when focusing on thyroid hormones, before starting a drug treatment with antidepressants of mood stabilizers. A second suggestion that arise from this review is that thyroid augmentation strategy should be worth considering before changing a drug class or else. The rate of thyroid augmentation employment in everyday practice is quite low (Chakrabarti and Malhotra 2001): we here report strong evidence-based suggestion to invert this trend.

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