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Review of the literature

The effects of ghrelin on sleep, appetite, and memory, and its possible role in depression: A review of the literature

Effets de la ghréline sur le sommeil, l'appétit, la mémoire et son possible rôle dans la dépression : une revue de la littérature

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ABSTRACT

Objectives. – Ghrelin is an orexigenic digestive hormone that plays a role in sleep and memory. Our work aims is to synthesize the effects of ghrelin on appetite, sleep and memory, and also to evidence its role in depressive disorders.
Methods. – A systematic search was carried out on PubMed with no time boundaries. The following MeSH terms were used: ghrelin AND (appetite regulation OR obesity), (sleep wake disorders OR sleep) (memory OR cognition disorders) (depression OR depressive disorder OR mood disorder).
Results. – Ghrelin triggers appetite and alters meal patterns by making them longer and richer. This can lead to pathologies, obesity and insulin-resistance. Ghrelin seems to have a favourable effect on sleep in human beings. It tends to make sleep more efficacious and better quality. Finally, it seems to have an effect on synaptic plasticity in the zones involved in memory and it has been shown to improve memory capacity in rodents. Regarding depression, the administration of ghrelin leads to an anti-depressive effect in animals and in humans. Conversely, post anti-depressant ghrelin titrations have generally shown a decrease in ghrelin levels. Resistant patients seem to retain high levels. Finally, the seriousness of depression could be related to ghrelin levels.
Conclusion. – Ghrelin plays a probable part in depression, especially for particular endophenotypes. A better understanding of ghrelin in depression could potentially help to optimize future therapeutic treatments.

Mots clés :
Ghréline
Sommeil
Appétit
Mémoire
Dépression

RÉSUMÉ

Objectifs. – La ghréline est une hormone digestive oréxigène, possédant un rôle dans le sommeil et la mémoire. Notre travail cherche à synthétiser l'effet de la ghréline sur l'appétit, le sommeil et la mémoire mais aussi à mettre en évidence son rôle dans le trouble dépressif.
Méthodes. – Une recherche systématique sur la base de données PubMed a été réalisée sans borne de durée. Les termes MeSH suivants ont été utilisés : ghrelin AND (appetite regulation OR obesity), (sleep wake disorders OR sleep) (memory OR cognition disorders) (depression OR depressive disorder OR mood disorder).

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Résultats. – La ghréline initie l'appétit et modifie les repas : plus longs et plus riches, Ceci pouvant s'avérer pathologiques et pourvoyeurs d'obésité et d'insulino-résistance. La ghréline semble avoir un effet promoteur du sommeil chez l'homme. Elle tend à rendre le sommeil plus efficace et de meilleure qualité. Enfin, elle paraît agir sur la plasticité synaptique dans les zones impliquées dans la mémoire et améliore les capacités mnésiques des rongeurs. Sur la dépression, l'administration de ghréline entraîne un effet antidépresseur chez l'animal ou chez l'homme. De manière opposée, les dosages de ghréline après traitement antidépresseur ont globalement montré une diminution des taux. Les patients résistants garderaient des taux élevés. Enfin, la gravité pourrait être positivement corrélée aux taux de ghréline.
Conclusion. – La ghréline a un rôle probable dans la dépression, notamment en fonction d'endophénotypes particuliers. Une meilleure compréhension de la ghréline dans la dépression pourrait potentiellement permettre d'optimiser nos prises en charge thérapeutiques futures.

1. Introduction

Ghrelin is a digestive hormone that was discovered to have orexigenic properties [1].

For this reason, it has been the subject of a number of studies focusing on the physio-pathological mechanisms of appetite [2–4]. Ghrelin has therefore been tested as a therapeutic target for a number of pathologies, and first of all obesity [5].

In addition, some authors have suggested the implication of ghrelin in sleep [6] and memory [7]. Consequently, ghrelin could be involved in a number of neurological illnesses. In Parkinson's disease, studies have shown that ghrelin has a protective role on dopaminergic neurons via an inhibition of the activation of the microglia [8]. In Alzheimer's disease, studies on mice have shown an improvement in memory disorders after administering ghrelin. Ghrelin seems to have a protective role against the toxicity of beta-amyloid plaques [9].

Appetite, sleep and memory are three subjects of interest in the field of research in psychiatry and more specifically in mood disorders. They are indeed three symptoms that are both frequent and easily identifiable during thymic episodes.

Depression is a major concern in terms of public health worldwide [10]. It is a frequent illness with a lifetime prevalence of 17% and a one-year prevalence of 6%. The World Health Organisation believes that, in the burden of illness across the world, the share of depression will increase from third place in 2004 to first place in 2030 [10].

Characteristic depressive episodes are often accompanied by sleep, appetite and memory alterations (DSM-5), three symptoms that are linked to the effects of ghrelin.

In the last 60 years, antidepressant therapies, with their effect on monoaminergic pathways, have drastically changed the way this illness is treated and our understanding of its physiopathology. Nevertheless, there are known limitations to these treatments. In recent years, the monoaminergic paradigm has been re-examined and new avenues of research have been developed after the antidepressant effect of ketamine was discovered [11].

For the above reasons, we focused on the effects of ghrelin on depression.

Our research aimed to review the effect of ghrelin on appetite, sleep and memory and to evidence its potential role as treatment for these three symptoms of depression or even as an active antidepressant.

2. Material and methods

A systematic search on PubMed was carried out in August 2016 with no time boundaries. The Guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used for this literature review [12]. The following MeSH terms were selected with no time limits: ghrelin AND (appetite regulation OR obesity), (sleep wake disorders OR sleep) (memory OR cognition disorders) (depression OR depressive disorder OR mood disorder).

Eligibility criteria for the review articles selected from PubMed/Medline databases were the following: English or French language and clinical or pre-clinical study. Literature reviews were also selected but were not directly part of the present literature review. Studies that were not selected in this way but were mentioned in article bibliographies were also reviewed to determine their eligibility. This method enabled the search to be extended to articles for which referencing errors had occurred, or because they were not mentioned on PubMed/Medline databases, but on another scientific literature database. The search initially identified 138 articles for the terms ghrelin (sleep wake disorders OR sleep), 71 for ghrelin AND (memory OR cognition disorders) and 45 for ghrelin AND (depression OR depressive disorder OR mood disorder). A method of double perusal using PRISMA guidelines enabled the selection of 15 articles for sleep [ghrelin AND (sleep wake disorders OR sleep)], 19 for memory [ghrelin AND (memory OR cognition disorders)], and 12 for depression [ghrelin AND (depression OR depressive disorder or mood disorder)]. A specific search process was reserved for research based on the MeSH terms ghrelin AND (appetite regulation OR obesity). These terms identified 1301 articles. A double perusal enabled us to identify the most relevant articles on the following basis: the factor impact of the journal, contribution in terms of physiological mechanisms, and consideration of the particular themes. Finally, 23 articles were selected for their results on appetite.

The results presented were derived from a double selection and perusal, thus guaranteeing a low risk of information loss.

3. Review of the literature

3.1. Effects on appetite

3.1.1. The psychopathology of ghrelin for appetite

Ghrelin is a digestive hormone composed of 28 amino acids. Kojima et al. isolated it and described it in 1999 [13]. It is mainly secreted by the stomach, and GHSR1 (Growth Hormone Secretagogue Receptor 1) is its specific receptor [14]. It is present in human plasma in two forms: one inactive form called unacylated ghrelin and an active form called acylated ghrelin synthesized by the action of an enzyme called GOAT (Ghrelin O-Acyl Transferase). The literature reports on a complex Ghrelin/GOAT/GHSR system involved in metabolic and energetic regulations enabling homeostasis to be maintained [15].

Ghrelin is considered as the antagonist of leptin, a hormone which, when secreted, induces satiety. The pattern of ghrelin secretion varies through the meal: its level increases before mealtimes [3] and decreases after [4].

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