

Drugs and HPA axis

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Abstract This paper outlines the interferences of the most widely used drugs with hypothalamo-pituitary-adrenal function and the related laboratory parameters, with the purpose of providing practical help to clinicians during testing for hypo- or hypercortisolemic states.

Keywords Drugs · HPA axis · Cortisol · ACTH · Urinary free cortisol

Introduction

Clinicians should always be aware of potential interactions between drugs and the hypothalamo-pituitary-adrenal (HPA) axis as these may modify parameters used for clinical assessment of its functional status. Accurate investigation of present and past drug history is therefore necessary to avoid misdiagnosis and inappropriate treatments. This treatise will review drug-induced changes in hormone measurements used for the diagnostic work-up for hypo- or hypercortisolemic states, starting with synthetic glucocorticoids and drugs used for treatment of Cushing's syndrome, then proceeding on to interferences of other pharmacological agents with parameters of HPA function in basal conditions and upon dynamic testing.

Synthetic glucocorticoids

Synthetic glucocorticoids exert a multitude of effects on almost every organ system and rank among the most

widely used drugs. They are employed in a variety of non-endocrine diseases (e.g., rheumatic, renal, allergic, asthmatic, ocular, skin, gastrointestinal, infectious, hepatic disorders), in addition to their use as replacement therapy for adrenal insufficiency. Two kinds of side effects should be kept in mind during the use of glucocorticoids: one resulting from continued use of supraphysiological doses, i.e. iatrogenic Cushing's syndrome, and the other secondary to drug withdrawal, i.e. HPA suppression.

Iatrogenic Cushing's syndrome, the most common form of hypercortisolism, is a unique disorder in which clinical features and biochemical changes typical of endogenous hypercortisolism, coexist with suppression of the HPA axis. Development of Cushingoid features is closely related to the dose and potency of the administered steroid as well as to the length of treatment, whereas the route of drug administration does not seem to be of primary importance. Indeed, even the development of iatrogenic Cushing's syndrome due to topical ocular steroids has been reported [1, 2]. Another interesting example of iatrogenic Cushing's syndrome are HIV-infected patients on inhaled corticosteroids, such as fluticasone, and protease-inhibiting antiretroviral drugs, such as ritonavir [3]. This association inhibits steroid hepatic metabolism and increases steroid bioavailability, thereby causing Cushingoid features and secondary adrenal insufficiency. Iatrogenic Cushing's syndrome has also been reported in a few patients treated with inhaled glucocorticoids and drugs such as itraconazole and clarithromycin, which inhibit hepatic cytochrome P450 3A (CYP3A), thus increasing glucocorticoid bioavailability [4–6]. Continuous cutaneous application of glucocorticoid preparations (e.g., ointments) on injured skin may also cause the development of iatrogenic Cushing's syndrome [7–9]. In the abovementioned circumstances, measurement of serum and urinary cortisol will yield variably increased levels in patients

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administered cortisone, hydrocortisone, prednisone and prednisolone as these drugs cross-react in most cortisol assays. Conversely, cortisol levels will be low in patients on dexamethasone, which does not interfere with cortisol measurements. Both basal and stimulated ACTH plasma levels are invariably low on glucocorticoid therapy.

Abrupt cessation of prolonged treatment with suppressive doses of glucocorticoids may precipitate secondary adrenal insufficiency. Some risk factors for HPA axis suppression are well recognized, such as pharmacokinetics, biological potency and half-life, in addition to affinity of the steroid for the glucocorticoid receptor [10]. Parenteral glucocorticoid therapy is more likely to suppress the HPA axis than topical administration, such as inhaled or intra-articular steroids. A recent report even described secondary adrenal insufficiency in infants after protracted topical steroids for diaper rash [11]. On the whole, it is usually accepted that adrenal atrophy with attendant insufficiency develops in patients who received the equivalent of 30 mg/day hydrocortisone, 7.5 mg/day prednisolone or 0.75 mg/day dexamethasone or more, per os, for at least three weeks. In these cases, the laboratory shows low levels of serum and urinary cortisol and low plasma ACTH concentrations.

Drugs used for treatment of Cushing's syndrome

Medical therapy is usually employed to correct endogenous hypercortisolism after surgery has failed and can be targeted to the hypothalamus/pituitary, the adrenal glands or the glucocorticoid receptor. All agents that modulate corticotropin-releasing factor (CRH) or ACTH release (Table 1) may affect parameters of HPA activity although their efficacy in Cushing's disease is mostly anecdotal. In addition to drugs affecting neurotransmission, which will be discussed in detail below, a spate of new drugs has recently been proposed for treatment of ACTH-dependent Cushing's syndrome, including PPAR- γ agonists and recently developed somatostatin analogues. So far, no report on the possible changes in HPA function in

patients administered these compounds for diabetes, acromegaly, gastrointestinal tumors etc. has been published. Ketoconazole, the mainstay of medical therapy in Cushing's syndrome, and the other steroid synthesis inhibitors (Table 1) are employed also in other clinical conditions, e.g. mycoses, anesthesia and malignant neoplasms, and may lead to low serum cortisol and androgen levels. Administration of ketoconazole, however, does not seem to be accompanied by a compensatory increase of plasma ACTH, as occurs with other steroid synthesis inhibitors, allegedly due to a concomitant restraint of ACTH release [12]. Of note, the anesthetic etomidate has been implicated in stress-associated hypocortisolemia in critically ill patients [13, 14]. Mifepristone (RU-486), a potent antagonist of glucocorticoid and progesterone receptors, thwarts the negative glucocorticoid feedback thus increasing ACTH/cortisol secretion in healthy [15] and ill subjects [16–18]. Somatostatin analogues decrease plasma ACTH and serum cortisol levels in some patient with ACTH-secreting pituitary or ectopic tumors but not in normal subjects [19].

Baseline plasma ACTH and serum or salivary cortisol

Most studies on changes in HPA parameters refer to basal plasma ACTH and serum cortisol levels, while far fewer are the reports on hormonal values under dynamic conditions, i.e. provocative or inhibitory maneuvers. Measurement of plasma ACTH is a means to discriminate pituitary from adrenal hypo- and hyperfunction. Conversely, estimation of morning cortisol is used mainly for the diagnosis of adrenocortical insufficiency while late-night serum or salivary cortisol is employed in the diagnostic work-up of Cushing's syndrome.

Many drugs interfere with basal HPA activity and therefore affect the results of ACTH and cortisol measurement, with neurotransmitter-modulating drugs as the most frequent culprits. The effects of these compounds depend on the dose administered, the length of treatment and the underlying disorder as changes observed in healthy

Table 1 Drugs used for treatment of Cushing's syndrome

CRH/ACTH inhibitors

Serotonin antagonists: cyproheptadine, ketanserin, ritanserin, metergoline

Dopaminergic agonists: bromocriptine, cabergoline

Catecholamine depletors: reserpine

GABAergic agents: valproic acid

Somatostatin analogues: octreotide, lanreotide, pasireotide

Peroxisome proliferator-activated receptor (PPAR- γ) agonists: pioglitazone, rosiglitazone

Steroid synthesis inhibitors

Single enzyme inhibitors: metyrapone, trilostane

Multiple enzyme inhibitors: mitotane, aminoglutethimide, ketoconazole, fluconazole, etomidate

Glucocorticoid receptor antagonists

Mifepristone (RU486)

subjects may differ from those observed in patients with psychiatric or other disorders. Clinicians should also take note of patients' behavioral habits, such as smoking or alcohol intake, with the excess of the latter as a well-known cause of clinical and/or biochemical pseudoCushing. Further, cigarette smoking appears to be associated with abrupt increases in cortisol levels whereas a cortisol decline is observed upon ceasing to smoke [20]. Measurement of basal ACTH and/or cortisol secretion is usually the first step of the diagnostic work-up and careful case history is therefore mandatory.

Serotonergic agonists and antagonists

Serotonin receptor agonists, commonly used as appetite suppressors, anxiolytic and antidepressants, mostly stimulate HPA axis, as has been observed with fenfluramine at high doses (i.e. above 30 mg/die p.o.) [21, 22], azapirones [23–26], sertraline [27] and flesinoxan [28]. These effects appear dose-dependent, as shown for the selective serotonin reuptake inhibitor (SSRI) citalopram [29, 30], and subject to tachyphylaxis [31]. No increase in basal ACTH and cortisol levels has been reported with another SSRI, fluoxetine, administered to normal volunteers [32, 33]. Of note, the serotonin-mediated activation on HPA function is blunted in chronic fatigue syndrome, a condition which may mimic adrenal insufficiency [34]. Ecstasy (i.e., 3,4-methylenedioxyamphetamine or MDMA) [35], its less toxic derivative 3,4-methylenedioxyethamphetamine (MDE) [36] and meta-chlorophenylpiperazine (*m*-CPP) [37] induce a marked rise in serum cortisol concentrations, possibly due to their effect on serotonin neurons. As for serotonin antagonists, in addition to those mentioned previously (see Table 1), atypical antidepressants trazodone [38] and etoperidone [39] have been shown to inhibit HPA activity in normal volunteers.

Dopaminergic agonists and antagonists

Both dopaminergic agonists, e.g., apomorphine [40], lergotriole [41], and antagonists, e.g. metoclopramide [42–44], fluphenazine [45], have been reported to enhance plasma ACTH and serum cortisol concentrations in normal subjects as well as in various clinical conditions, including schizophrenia and prolactin-secreting tumors. In healthy women, however, the ACTH and cortisol increase induced by metoclopramide appears restricted to the mid-luteal phase as no changes were observed during the early and late follicular phase [46]. A similar observation has been reported in one study with methylphenidate [47] although not confirmed by another [48]. Interestingly, dopaminergic agonists bromocriptine and cabergoline may decrease ACTH/cortisol secretion in patients with Cushing's

disease. Acute levodopa administration, used in tandem with the peripheral DOPA decarboxylase inhibitor benzerazide, appears to lower serum cortisol levels in patients with Parkinson's disease [49] while haloperidol, a well-known antipsychotic, does not affect HPA activity in healthy subjects [50]. Lastly, the alkaloid cocaine, which is known to inhibit dopamine uptake, can also increase cortisol values in healthy individuals [51].

Adrenergic agonists and antagonists

The alpha 2 receptor agonist clonidine has been shown to reduce cortisol levels in several studies, including those on obese and hypertensive individuals [52–54]. Likewise, an ACTH and cortisol decrease has been observed during clonidine testing in children with short stature [55]. Conversely, alpha 2 receptor antagonists such as yohimbine and idazoxan appear to increase cortisol levels [56]. The antidepressant reboxetine, a selective noradrenaline reuptake inhibitor, also significantly stimulates HPA activity [57] with more pronounced effects in males compared with females [58]. Amphetamine, a central sympathomimetic amine, induces a short-lasting rise in cortisol levels in normal subjects [59] whereas a paradoxical suppression can be observed in depressed patients [60].

Opiate agonists and antagonists

Complete and partial agonists or mixed opiate agonist-antagonists, such as the antidiarrheal loperamide [61], the analgesics morphine, methadone, pentazocine and nalorphine [62], buprenorphine [63], codeine [64], and the recreational drug heroin [65] significantly suppress basal serum cortisol levels. This has been documented in normal subjects, patients with anorexia [66], Addison's disease [67], pituitary disease (acromegaly, prolactinoma, pituitary dwarfism) [68], obesity [69], polycystic ovary syndrome [70] or psychiatric ailments [71]. Conversely, spiradoline, a recently developed kappa receptor agonist, stimulates cortisol secretion dose-dependently, in keeping with different actions of opioid receptor subtypes on the HPA axis [72]. As expected, opioid antagonists naloxone [73], naltrexone [74] and nalmefene [75] increase both plasma ACTH and serum cortisol concentrations in healthy individuals as well as in patients with bulimia [76], acromegaly [77], obesity [78], alcohol abuse [79] or mood disorders [80]. A less pronounced increase compared with normal subjects has been observed in patients with Nelson's syndrome [81], Alzheimer's [82] or Parkinson's disease [83], whereas patients with polycystic ovary syndrome exhibit a more marked increase after naloxone administration [84]. Of note, the ACTH and cortisol increase induced by naltrexone is particularly marked in alcohol-dependent subjects [85].

GABAergic agonists

Valproic acid, the anticonvulsant GABAergic agonist, does not affect ACTH/cortisol secretion in the short term [86] but has been found to decrease basal ACTH/cortisol secretion during protracted administration in epileptic patients [87, 88] and, due to this action, has been used with variable effects in Cushing's disease and Nelson's syndrome [89]. Of note, valproic acid has also been shown to inhibit steroid biosynthesis by acting upon 3β -hydroxydehydrogenase [90], an effect that has been linked to the increased incidence of polycystic ovary syndrome in patients on chronic treatment [91]. The central GABAergic system appears to be involved in the HPA suppressive effect of benzodiazepines, e.g., temazepam [92], alprazolam [93], thus interruption of these psychoactive drugs is recommended prior to testing HPA function. Clinicians should also be aware that secondary adrenal failure may develop in patients on long-term treatment with benzodiazepines, as recently reported with flunitrazepam [94].

Cholinergic agents

The cholinesterase inhibitor physostigmine, used to counteract poisoning by anticholinergic drugs or plants, is associated with an increase in plasma ACTH and serum cortisol concentrations in healthy subjects [95, 96] and in patients with Alzheimer's disease [97, 98] or major depression [99]. Elderly subjects and men appear more sensitive to this effect compared with younger subjects and women [100, 101].

Miscellaneous psychotropic drugs

Antipsychotic drugs such as olanzapine and quetiapine, which antagonize serotonin, dopamine and histamine receptors, appear to reduce HPA activity in healthy subjects [50]. In contrast, tricyclic antidepressants such as desimipramine [102], imipramine [103] and clomipramine [104, 105] enhance ACTH and cortisol release in a dose-dependent manner. Mirtazapine, a recently developed antidepressant which antagonizes serotonin, histamine and alpha 2 adrenergic receptors, reduces cortisol levels in healthy subjects [106] as well as in anorexic [107] and depressed patients [108].

Immunomodulatory and hormonal drugs

Cytokines, such as interferons (IFN), interleukins (IL) and tumor necrosis factor (TNF), stimulate HPA axis and, indeed, immunotherapy for cancer or chronic hepatitis increase ACTH and cortisol levels [109]. This can be seen after acute or chronic administration of IFN-alpha [110], IFN-beta [111], IFN-gamma [112], TNF-alpha [113] and

IL-1 alpha and beta [114], IL-2 [115] and IL-6 [116]. However, not all cytokines exert the same effect, as IL-3 administration may blunt the IL-2-induced cortisol increase [117].

Among hormonal compounds, growth hormone (GH) and thyroid hormones may interfere with HPA function. During recombinant human (rh) GH replacement therapy, morning serum cortisol levels significantly declined in adult GH-deficient patients with preserved HPA activity [118]. Patients with thyrotoxicosis display higher plasma ACTH concentrations and free cortisol index (serum cortisol/CBG) values compared with euthyroid subjects [119]. Furthermore, long-lasting severe thyrotoxicosis is associated with a reversible attenuation of the adrenal response to an acute challenge [120]. Medroxyprogesterone acetate (MPA) and megestrol, synthetic progestational agents used in the treatment of endometriosis, hirsutism and metastatic breast cancer, interact with the glucocorticoid receptor, and their long-term administration may result in Cushingoid features and suppression of ACTH and cortisol secretion. This has been shown to occur in healthy subjects [121, 122] as well as cancer [123–125] and AIDS patients [125, 126]. In this context it is worth recalling that estrogens increase cortisol-binding globulin synthesis thereby leading to a variable elevation of serum cortisol [127]. This effect is more apparent with oral estrogen preparations and might be insignificant with transdermal patches [128]. Conversely, long-term administration of the selective estrogen receptor modulator raloxifene is reported to decrease cortisol levels and increase ACTH levels in postmenopausal women [129]. Interestingly, the cholecystokinin 8-like peptide ceruletide, used for paralytic ileus and pancreatic malfunction, stimulates ACTH and cortisol secretion [130] as does the antidepressant herb mixture *Hypericum perforatum* (St. John's Wort) [131]. Lastly, desmopressin, the long-acting analogue of arginin vasopressin, elicits the release of ACTH and cortisol in patients with Cushing's disease but not in the majority of normal, obese and depressed subjects [132].

Urinary free cortisol, midnight cortisol and dynamic tests of adrenal function

In the absence of specific studies, it can be assumed that the effects of different drugs, as reported in the previous chapters, also apply to the estimation of urinary free cortisol, midnight serum cortisol and to the dynamic exploration of the HPA function.

Urinary free cortisol

Urinary free cortisol (UFC) is widely used to screen for Cushing's syndrome using radioimmunoassays (RIA) or

the more specific high performance liquid chromatography (HPLC) and false results may be caused by drugs that interfere with the assay or with HPA function. Synthetic steroids variably cross-react with antibodies used in cortisol RIA assays and may lead to over- or underestimation of UFC measurements [133, 134] and some, such as prednisolone [135], may coelute with cortisol even on HPLC. Falsely elevated values due to coelution have been reported also for carbamazepine [135, 136] and digoxin [135] but this problem can apparently be overcome with HPLC coupled to tandem mass spectrometry (HPLC-MS/MS) [137]. Fenofibrate, a lipid-lowering agent, also interferes with cortisol measurement at HPLC and a double HPLC-MS/MS is required for precise measurement [138]. As regards direct drug effects on UFC excretion, an increase in UFC has been observed in subjects on fenfluramine (180 mg/daily) [139] or chronic use of the narcotic γ -hydroxybutyric acid [140] while a reduction is apparent in patients taking benzodiazepines [141, 142] or mirtazapine [106, 143]. Unlike serum cortisol, UFC measurements seem unaffected by estrogen replacement [144] or oral contraceptive administration [145].

Licorice administration may mimic mineralocorticoid excess (hypertension and hypokalemia) and is associated with an increase in UFC due to inhibition of 11β -hydroxysteroid dehydrogenase type 2, the isoenzyme which converts cortisol to cortisone [146]. In contrast, rhGH replacement therapy was associated with significant reduction in UFC levels in adult patients with GH deficiency [118], likely through inhibition of 11β -hydroxysteroid dehydrogenase type 1, which converts cortisone to cortisol [147].

Dexamethasone suppression tests

Dexamethasone suppression test is of decisive importance for the diagnosis and differential diagnosis of Cushing's syndrome and relies on the sensitivity of the hypothalamo-pituitary unit to the negative feedback from exogenous glucocorticoids. Dexamethasone, a synthetic long-acting glucocorticoid, is metabolized primarily by cytochrome P450 3A4 (CYP3A4), which is responsible for the metabolism of a large number of xenobiotics. Agents that increase hepatic CYP3A4 activity, such as carbamazepine [148], phenytoin [149], rifampicin [150], barbiturates [151, 152] and, recently, St. John's Wort [153, 154] accelerate dexamethasone clearance and hence cause false positive results (lack of inhibition). Of note, false positive results occur mostly with the low dose dexamethasone suppression tests (1 mg or 2 mg overnight) whereas the suppressibility by high dose dexamethasone appears to be maintained in patients with Cushing's disease [155]. Other drugs which may lead to falsely high post-dexamethasone cortisol values are cholinergic agents such as physostigmine and the

muscarinic agonist arecoline [156, 157], serotonergic agonists, e.g., buspirone [158], citalopram [159], the GABAergic γ -hydroxybutyric acid [140] and the lithium-tricyclic antidepressant association [160]. Of note, this effect by lithium could mask recovery of cortisol suppressibility by low doses of dexamethasone, an index of favorable outcome in depressed patients treated with antidepressants [161].

As mentioned previously, estrogen administration leads to increased serum cortisol levels and these may be increased to the Cushingoid range even after dexamethasone [127, 162, 163]. Salivary cortisol is recommended if estrogens cannot be withdrawn [164].

Midnight serum or salivary cortisol

Midnight serum cortisol, another mainstay of the diagnosis of Cushing's syndrome, is increased during antidepressant treatment with mirtazapine [165], clomipramine [166], desimipramine [167], moclobemide (an inhibitor of monoamine oxidase A) [168], the antipsychotic olanzapine [169] and the SSRI inhibitor fluvoxamine [167]. Late-night cortisol is also increased by the antimineralocorticoid canrenoate [170]. Conversely, nocturnal cortisol secretion is reduced by the tricyclic antidepressant trimipramine [171–173] as well as in heroin addicts [174].

ACTH stimulation test

The ACTH stimulation test is used to assess adrenocortical reserve in primary and secondary adrenal insufficiency and the cortisol response may be abnormally reduced in patients on paroxetine and sertraline, two SSRI inhibitors [175]. Likewise, low cortisol responses to ACTH have been registered in subjects on MPA or megestrol [176–178] as well as in patients with organic GH deficiency on rhGH therapy although not in children with idiopathic isolated GH deficiency [179]. The same trend of response may be documented in patients requiring antifungal steroid synthesis inhibitors such as ketoconazole [180] or high-dose fluconazole [181]. Conversely, the β -adrenergic antagonist propranolol seems to enhance the cortisol elevation induced by ACTH [182] as well as by CRH [183].

Corticotropin-releasing hormone stimulation test

The CRH test is employed in the differential diagnosis of Cushing's syndrome (distinction between ACTH-dependent and independent forms and, within the former, between Cushing's disease and ectopic ACTH secretion) and to disclose adrenal insufficiency secondary to ACTH deficiency.

Cortisol concentrations after CRH stimulation are higher in patients on citalopram [184], propranolol [182, 185], canrenoate [186] or metoclopramide [187]. Interferon alpha likewise enhances the ACTH and cortisol response to CRH in cancer patients [188]. Conversely, opiates such as morphine attenuate the CRH-induced ACTH and cortisol release [189, 190], as do imipramine [191] and temazepam [192]. Interestingly, in patients with Cushing's disease, the CRH response is unaffected by temazepam [192].

Conclusions

A number of drugs can impair the laboratory assessment of HPA function either influencing ACTH/cortisol secretion, and hence their peripheral concentrations, or interfering with hormonal assays. Careful drug history should always be obtained whenever HPA activity has to be evaluated.

References

- Afandi B, Toumeh MS, Saadi HF (2003) Cushing's syndrome caused by unsupervised use of ocular glucocorticoids. *Endocr Pract* 9:526–529
- Chiang MY, Sarkar M, Koppens JM, Milles J, Shah P (2006) Exogenous Cushing's syndrome and topical ocular steroids. *Eye* 20:725–727. doi:10.1038/sj.eye.6701956
- Pessanha TM, Campos JM, Barros AC, Pone MV, Garrido JR, Pone SM (2007) Iatrogenic Cushing's syndrome in a adolescent with AIDS on ritonavir and inhaled fluticasone. Case report and literature review. *AIDS* 21(4):529–532
- Main KM, Skov M, Sillesen IB et al (2002) Cushing's syndrome due to pharmacological interaction in a cystic fibrosis patient. *Acta Paediatr* 91:1008–1011. doi:10.1080/080352502760272759
- De Wachter E, Malfrout A, De Schutter I, Vanbesien J, De Schepper J (2003) Inhaled budesonide induced Cushing's syndrome in cystic fibrosis patients, due to drug inhibition of cytochrome P450. *J Cyst Fibros* 2:72–75. doi:10.1016/S1569-1993(03)00022-5
- Bolland MJ, Bagg W, Thomas MG, Lucas JA, Ticehurst R, Black PN (2004) Cushing's syndrome due to interaction between inhaled corticosteroids and itraconazole. *Ann Pharmacother* 38:46–49. doi:10.1345/aph.1D222
- Halverstam CP, Vachharajani A, Mallory SB (2007) Cushing syndrome from percutaneous absorption of 1% hydrocortisone ointment in Netherton syndrome. *Pediatr Dermatol* 24:42–45
- Ermis B, Ors R, Tastekin A, Ozkan B (2003) Cushing's syndrome secondary to topical corticosteroids abuse. *Clin Endocrinol (Oxf)* 58:795–796. doi:10.1046/j.1365-2265.2003.18021.x
- Abma EM, Blanken R, De Heide LJ (2002) Cushing's syndrome caused by topical steroid therapy for psoriasis. *Neth J Med* 60:148–150
- Hopkins RL, Leinung MC (2005) Exogenous Cushing's syndrome and glucocorticoid withdrawal. *Endocrinol Metab Clin North Am* 34:371–384. doi:10.1016/j.ecl.2005.01.013
- Güven A, Gülümser O, Ozgen T (2007) Cushing's syndrome and adrenocortical insufficiency caused by topical steroids: misuse or abuse? *J Pediatr Endocrinol Metab* 20:1173–1182
- Loli P, Berselli ME, Tagliaferri M (1986) Use of ketoconazole in the treatment of Cushing's syndrome. *J Clin Endocrinol Metab* 63:1365–1371
- Mistraletti G, Donatelli F, Carli F (2005) Metabolic and endocrine effects of sedative agents. *Curr Opin Crit Care* 11:312–317. doi:10.1097/01.ccx.0000166397.50517.1f
- Absalom A, Pledger D, Kong A (1999) Adrenocortical function in critically ill patients 24 h after a single dose of etomidate. *Anaesthesia* 54:861–867. doi:10.1046/j.1365-2044.1999.01003.x
- Bertagna X, Escourolle H, Pinquier JL et al (1994) Administration of RU 486 for 8 days in normal volunteers: antigluco-corticoid effect with no evidence of peripheral cortisol deprivation. *J Clin Endocrinol Metab* 78:375–380. doi:10.1210/jc.78.2.375
- Flores BH, Kenna H, Keller J, Solvason HB, Schatzberg AF (2006) Clinical and biological effects of mifepristone treatment for psychotic depression. *Neuropsychopharmacology* 31:628–636. doi:10.1038/sj.npp.1300884
- Pomara N, Hernando RT, de la Pena CB, Sidtis JJ, Cooper TB, Ferris S (2006) The effect of mifepristone (RU 486) on plasma cortisol in Alzheimer's disease. *Neurochem Res* 31:585–588. doi:10.1007/s11064-006-9055-5
- Heikinheimo O, Ranta S, Grunberg S, Lähteenmäki P, Spitz IM (1997) Alterations in the pituitary-thyroid and pituitary-adrenal axes – consequences of long-term mifepristone treatment. *Metabolism* 46:292–296. doi:10.1016/S0026-0495(97)90256-0
- Diez JJ, Iglesias P (2007) Pharmacological therapy of Cushing's syndrome: drugs and indications. *Mini Rev Med Chem* 7:467–480. doi:10.2174/138955707780619653
- Steptoe A, Ussher M (2006) Smoking, cortisol and nicotine. *Int J Psychophysiol* 59:228–235. doi:10.1016/j.ijpsycho.2005.10.011
- Coccaro EF, Kavoussi RJ, Cooper TB, Hauger RL (1996) Hormonal responses to d- and d,l-fenfluramine in healthy human subjects. *Neuropsychopharmacology* 15:595–607. doi:10.1016/S0893-133X(96)00133-9
- Schurmeyer TH, Brademann G, von zur Muhlen A (1996) Effect of fenfluramine on episodic ACTH and cortisol secretion. *Clin Endocrinol (Oxf)* 45:39–45. doi:10.1111/j.1365-2265.1996.tb02058.x
- Cleare AJ, Forsling M, Bond AJ (1998) Neuroendocrine and hypothermic effects of 5-HT1A receptor stimulation with ipsapirone in healthy men: a placebo-controlled study. *Int Clin Psychopharmacol* 13:23–32. doi:10.1097/00004850-199801000-00004
- Meltzer HY, Maes M (1994) Effects of buspirone on plasma prolactin and cortisol levels in major depressed and normal subjects. *Biol Psychiatry* 35:316–323. doi:10.1016/0006-3223(94)90035-3
- Walsh AE, Ware CJ, Cowen PJ (1991) Lithium and 5-HT1A receptor sensitivity: a neuroendocrine study in healthy volunteers. *Psychopharmacology (Berl)* 105:568–572. doi:10.1007/BF02244382
- Rausch JL, Stahl SM, Hauger RL (1990) Cortisol and growth hormone responses to the 5-HT1A agonist gepirone in depressed patients. *Biol Psychiatry* 28:73–78. doi:10.1016/0006-3223(90)90434-4
- Sagud M, Pivac N, Muck-Seler D, Jakovljevic M, Mihaljevic-Peles A, Korsic M (2002) Effects of sertraline treatment on plasma cortisol, prolactin and thyroid hormones in female depressed patients. *Neuropsychobiology* 45:139–143. doi:10.1159/000054954
- Pitchot W, Wauthy J, Hansenne M et al (2002) Hormonal and temperature responses to the 5-HT1A receptor agonist flesinoxan in normal volunteers. *Psychopharmacology (Berl)* 164:27–32. doi:10.1007/s00213-002-1177-0

29. Bhagwagar Z, Hafizi S, Cowen PJ (2002) Acute citalopram administration produces correlated increases in plasma and salivary cortisol. *Psychopharmacology (Berl)* 163:118–120. doi: [10.1007/s00213-002-1149-4](https://doi.org/10.1007/s00213-002-1149-4)
30. Lotrich FE, Bies R, Muldoon MF, Manuck SB, Smith GS, Pollock BG (2005) Neuroendocrine response to intravenous citalopram in healthy control subjects: pharmacokinetic influences. *Psychopharmacology (Berl)* 178:268–275. doi: [10.1007/s00213-004-2006-4](https://doi.org/10.1007/s00213-004-2006-4)
31. Berlin I, Warot D, Legout V, Guillemand S, Schollhammer G, Puech AJ (1998) Blunted 5-HT_{1A}-receptor agonist-induced corticotropin and cortisol responses after long-term ipsapirone and fluoxetine administration to healthy subjects. *Clin Pharmacol Ther* 63:428–436. doi: [10.1016/S0009-9236\(98\)90038-8](https://doi.org/10.1016/S0009-9236(98)90038-8)
32. Lerer B, Gelfin Y, Gorfine M, Allolio B, Lesch KP, Newman ME (1999) 5-HT_{1A} receptor function in normal subjects on clinical doses of fluoxetine: blunted temperature and hormone responses to ipsapirone challenge. *Neuropsychopharmacology* 20:628–639. doi: [10.1016/S0893-133X\(98\)00106-7](https://doi.org/10.1016/S0893-133X(98)00106-7)
33. Torpy DJ, Grice JE, Hockings GI, Walters MM, Crosbie GV, Jackson RV (1997) Diurnal effects of fluoxetine and naloxone on the human hypothalamic-pituitary-adrenal axis. *Clin Exp Pharmacol Physiol* 24:421–423. doi: [10.1111/j.1440-1681.1997.tb01213.x](https://doi.org/10.1111/j.1440-1681.1997.tb01213.x)
34. Dinan TG, Majeed T, Lavelle E, Scott LV, Berti C, Behan P (1997) Blunted serotonin-mediated activation of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome. *Psychoneuroendocrinology* 22:261–267. doi: [10.1016/S0306-4530\(97\)00002-4](https://doi.org/10.1016/S0306-4530(97)00002-4)
35. de la Torre R, Farre M, Roset PN et al (2000) Pharmacology of MDMA in humans. *Ann N Y Acad Sci* 914:225–237
36. Gouzoulis-Mayfrank E, Thelen B, Habermeyer E et al (1999) Psychopathological, neuroendocrine and autonomic effects of 3,4-methylenedioxyethylamphetamine (MDA), psilocybin and d-methamphetamine in healthy volunteers. Results of an experimental double-blind placebo-controlled study. *Psychopharmacology (Berl)* 142:41–50. doi: [10.1007/s002130050860](https://doi.org/10.1007/s002130050860)
37. Feuchtl A, Bagli M, Stephan R et al (2004) Pharmacokinetics of m-chlorophenylpiperazine after intravenous and oral administration in healthy male volunteers: implication for the pharmacodynamic profile. *Pharmacopsychiatry* 37:180–188. doi: [10.1055/s-2004-827175](https://doi.org/10.1055/s-2004-827175)
38. Monteleone P (1991) Effects of trazodone on plasma cortisol in normal subjects. A study with drug plasma levels. *Neuropsychopharmacology* 5:61–64
39. Costa A, Martignoni E, Blandini F, Petraglia F, Genazzani AR, Nappi G (1993) Effects of etoperidone on sympathetic and pituitary-adrenal responses to diverse stressors in humans. *Clin Neuropharmacol* 16:127–138. doi: [10.1097/00002826-199304000-00005](https://doi.org/10.1097/00002826-199304000-00005)
40. Jezova D, Vigas M (1988) Apomorphine injection stimulates beta-endorphin, adrenocorticotropin, and cortisol release in healthy man. *Psychoneuroendocrinology* 13:479–485. doi: [10.1016/0306-4530\(88\)90033-9](https://doi.org/10.1016/0306-4530(88)90033-9)
41. Thorner MO, Ryan SM, Wass JA et al (1978) Effect of the dopamine agonist, lergotril mesylate, on circulating anterior pituitary hormones in man. *J Clin Endocrinol Metab* 47:372–378
42. Nishida S, Matsuki M, Nagase Y et al (1983) Stress-mediated effect of metoclopramide on cortisol secretion in man. *J Clin Endocrinol Metab* 56:839–843
43. Staessen J, Fiocchi R, Bouillon R et al (1985) Differential responses of plasma aldosterone, cortisol and adrenocorticotropin to two dopamine receptor antagonists. *Methods Find Exp Clin Pharmacol* 7:523–527
44. Coiro V, Volpi R, Capretti L et al (1990) 5-HT₁-, but not 5-HT₂-serotonergic, M₁-, M₂-muscarinic cholinergic or dopaminergic receptors mediate the ACTH/cortisol response to metoclopramide in man. *Horm Res* 33:233–238
45. Jakovljevic M, Pivac N, Mihaljevic-Peles A et al (2007) The effects of olanzapine and fluphenazine on plasma cortisol, prolactin and muscle rigidity in schizophrenic patients: a double blind study. *Prog Neuropsychopharmacol Biol Psychiatry* 31:399–402. doi: [10.1016/j.pnpbp.2006.10.007](https://doi.org/10.1016/j.pnpbp.2006.10.007)
46. Seki K (1989) Variability of cortisol and adrenocorticotrophic hormone responses to metoclopramide during the menstrual cycle. *Gynecol Obstet Invest* 27:201–203
47. Joyce PR, Donald RA, Nicholls MG, Livesey JH, Abbott RM (1986) Endocrine and behavioral responses to methylphenidate in normal subjects. *Biol Psychiatry* 21:1015–1023. doi: [10.1016/0006-3223\(86\)90282-9](https://doi.org/10.1016/0006-3223(86)90282-9)
48. Brown WA, Williams BW (1976) Methylphenidate increases serum growth hormone concentrations. *J Clin Endocrinol Metab* 43:937–939
49. Müller T, Muhlack S (2007) Acute levodopa intake and associated cortisol decrease in patients with Parkinson disease. *Clin Neuropharmacol* 30:101–106. doi: [10.1097/01.WNF.0000240954.72186.91](https://doi.org/10.1097/01.WNF.0000240954.72186.91)
50. Cohrs S, Roher C, Jordan W et al (2006) The atypical antipsychotics olanzapine and quetiapine, but not haloperidol, reduce ACTH and cortisol secretion in healthy subjects. *Psychopharmacology (Berl)* 185:11–18. doi: [10.1007/s00213-005-0279-x](https://doi.org/10.1007/s00213-005-0279-x)
51. Heesch CM, Negus BH, Keffer JH, Snyder RW II, Risser RC, Eichhorn EJ (1995) Effects of cocaine on cortisol secretion in humans. *Am J Med Sci* 310:61–64. doi: [10.1097/00000441-199508000-00004](https://doi.org/10.1097/00000441-199508000-00004)
52. Pende A, Musso NR, Montaldi ML, Arzese M, Vergassola C, Devilla L (1987) Interaction between morphine, an opioid agonist, and clonidine, an alpha-adrenergic agonist, on the regulation of anterior pituitary hormone secretion in normal male subjects. *Biomed Pharmacother* 41:243–247
53. Slowinska-Szrednicka J, Zgliczynski S, Soszynski P, Pucilowska J, Wierzbicki M, Jeske W (1988) Effect of clonidine on beta-endorphin, ACTH and cortisol secretion in essential hypertension and obesity. *Eur J Clin Pharmacol* 35:115–121. doi: [10.1007/BF00609239](https://doi.org/10.1007/BF00609239)
54. Baranowska B (1990) The effect of clonidine on hormone release mediated through activation of opiate receptors. *Cardiovasc Drugs Ther* 4:1113–1117. doi: [10.1007/BF01856507](https://doi.org/10.1007/BF01856507)
55. Munoz-Hoyos A, Fernandez-Garcia JM, Molina-Carballo A et al (2000) Effect of clonidine on plasma ACTH, cortisol and melatonin in children. *J Pineal Res* 29:48–53. doi: [10.1034/j.1600-079X.2000.290107.x](https://doi.org/10.1034/j.1600-079X.2000.290107.x)
56. Krystal JH, McDougale CJ, Woods SW, Price LH, Heninger GR, Charney DS (1992) Dose-response relationship for oral idazoxan effects in healthy human subjects: comparison with oral yohimbine. *Psychopharmacology (Berl)* 108:313–319. doi: [10.1007/BF02245117](https://doi.org/10.1007/BF02245117)
57. Schule C, Baghai T, Schmidbauer S, Bidlingmaier M, Strasburger CJ, Laakmann G (2004) Reboxetine acutely stimulates cortisol, ACTH, growth hormone and prolactin secretion in healthy male subjects. *Psychoneuroendocrinology* 29:185–200. doi: [10.1016/S0306-4530\(03\)00022-2](https://doi.org/10.1016/S0306-4530(03)00022-2)
58. Tse WS, Bond AJ (2005) Sex differences in cortisol response to reboxetine. *J Psychopharmacol* 19:46–50. doi: [10.1177/0269881105048896](https://doi.org/10.1177/0269881105048896)
59. Jacobs D, Silverstone T, Rees L (1989) The neuroendocrine response to oral dextroamphetamine in normal subjects. *Int Clin Psychopharmacol* 4:135–147
60. Sachar EJ, Halbreich U, Asnis GM, Nathan RS, Halpern FS, Ostrow L (1981) Paradoxical cortisol responses to dextroamphetamine in endogenous depression. *Arch Gen Psychiatry* 38:1113–1117

61. Auernhammer CJ, Stalla GK, Lange M, Pfeiffer A, Müller OA (1992) Effects of loperamide on the human hypothalamo-pituitary-adrenal axis in vivo and in vitro. *J Clin Endocrinol Metab* 75:552–557. doi:[10.1210/jc.75.2.552](https://doi.org/10.1210/jc.75.2.552)
62. Delitala G, Grossman A, Besser M (1983) Differential effects of opiate peptides and alkaloids on anterior pituitary hormone secretion. *Neuroendocrinology* 37:275–279
63. Pende A, Musso NR, Montaldi ML, Pastorino G, Arzese M, Devilla L (1986) Evaluation of the effects induced by four opiate drugs, with different affinities to opioid receptor subtypes, on anterior pituitary LH, TSH, PRL and GH secretion and on cortisol secretion in normal men. *Biomed Pharmacother* 40:178–182
64. Garland EJ, Zis AP (1989) Effect of codeine and oxazepam on afternoon cortisol secretion in men. *Psychoneuroendocrinology* 14:397–402. doi:[10.1016/0306-4530\(89\)90009-7](https://doi.org/10.1016/0306-4530(89)90009-7)
65. Rasheed A, Tareen IA (1995) Effects of heroin on thyroid function, cortisol and testosterone level in addicts. *Pol J Pharmacol* 47:441–444
66. Zis AP, Remick RA, Clark CM, Goldner E, Grant BE, Brown GM (1989) Effect of morphine on cortisol and prolactin secretion in anorexia nervosa and depression. *Clin Endocrinol (Oxf)* 30:421–427
67. Alolio B, Winkelmann W, Hipp FX, Kaulen D, Mies R (1982) Effects of a met-enkephalin analog on adrenocorticotropin (ACTH), growth hormone, and prolactin in patients with ACTH hypersecretion. *J Clin Endocrinol Metab* 55:1–7
68. Demura R, Suda T, Wakabayashi I et al (1981) Plasma pituitary hormone responses to the synthetic enkephalin analog (FK 33–824) in normal subjects and patients with pituitary diseases. *J Clin Endocrinol Metab* 52:263–266
69. Bernini GP, Argenio GF, Cerri F, Franchi F (1994) Comparison between the suppressive effects of dexamethasone and loperamide on cortisol and ACTH secretion in some pathological conditions. *J Endocrinol Invest* 17:799–804
70. Ciampelli M, Guido M, Cucinelli F, Cinque B, Barini A, Lanzone A (2000) Hypothalamic-pituitary-adrenal axis sensitivity to opioids in women with polycystic ovary syndrome. *Fertil Steril* 73:712–717. doi:[10.1016/S0015-0282\(99\)00602-0](https://doi.org/10.1016/S0015-0282(99)00602-0)
71. Banki CM, Arato M (1987) Multiple hormonal responses to morphine: relationship to diagnosis and dexamethasone suppression. *Psychoneuroendocrinology* 12:3–11. doi:[10.1016/0306-4530\(87\)90016-3](https://doi.org/10.1016/0306-4530(87)90016-3)
72. Ur E, Wright DM, Bouloux PM, Grossman A (1997) The effects of spiradoline (U-62066E), a kappa-opioid receptor agonist, on neuroendocrine function in man. *Br J Pharmacol* 120:781–784. doi:[10.1038/sj.bjp.0700971](https://doi.org/10.1038/sj.bjp.0700971)
73. Uhart M, Chong RY, Oswald L, Lin PI, Wand GS (2006) Gender differences in hypothalamic-pituitary-adrenal (HPA) axis reactivity. *Psychoneuroendocrinology* 31:642–652. doi:[10.1016/j.psyneuen.2006.02.003](https://doi.org/10.1016/j.psyneuen.2006.02.003)
74. Mendelson JH, Mello NK, Cristofaro P, Skupny A, Ellingboe J (1986) Use of naltrexone as a provocative test for hypothalamic-pituitary hormone function. *Pharmacol Biochem Behav* 24:309–313. doi:[10.1016/0091-3057\(86\)90356-4](https://doi.org/10.1016/0091-3057(86)90356-4)
75. Geer EB, Landman RE, Wardlaw SL, Conwell IM, Freda PU (2005) Stimulation of the hypothalamic-pituitary-adrenal axis with the opioid antagonist nalmefene. *Pituitary* 8:115–122. doi:[10.1007/s11102-005-5227-6](https://doi.org/10.1007/s11102-005-5227-6)
76. Coiro V, d'Amato L, Marchesi C et al (1990) Luteinizing hormone and cortisol responses to naloxone in normal weight women with bulimia. *Psychoneuroendocrinology* 15:463–470. doi:[10.1016/0306-4530\(90\)90069-L](https://doi.org/10.1016/0306-4530(90)90069-L)
77. Delitala G, Giusti M, Borsi L et al (1981) Effects of a Met-enkephalin analogue and naloxone infusion on anterior pituitary hormone secretion in acromegaly. *Horm Res* 15:88–98
78. Guido M, Ciampelli M, Fulghesu AM et al (1999) Influence of body mass on the hypothalamic-pituitary-adrenal-axis response to naloxone in patients with polycystic ovary syndrome. *Fertil Steril* 71:462–467. doi:[10.1016/S0015-0282\(98\)00470-1](https://doi.org/10.1016/S0015-0282(98)00470-1)
79. Kemper A, Koalick F, Thiele H, Retzow A, Rathsack R, Nickel B (1990) Cortisol and beta-endorphin response in alcoholics and alcohol abusers following a high naloxone dosage. *Drug Alcohol Depend* 25:319–326. doi:[10.1016/0376-8716\(90\)90158-B](https://doi.org/10.1016/0376-8716(90)90158-B)
80. Michelson D, Altemus M, Galliven E, Hill L, Greenberg BD, Gold P (1996) Naloxone-induced pituitary-adrenal activation does not differ in patients with depression, obsessive compulsive disorder, and healthy controls. *Neuropsychopharmacology* 15:207–212. doi:[10.1016/0893-133X\(95\)00210-5](https://doi.org/10.1016/0893-133X(95)00210-5)
81. Elias AN, Gwinup G, Valenta LJ (1981) Effects of valproic acid, naloxone and hydrocortisone in Nelson's syndrome and Cushing's disease. *Clin Endocrinol (Oxf)* 15:151–154
82. Tariot PN, Upadhyaya A, Sunderland T et al (1999) Physiologic and neuroendocrine responses to intravenous naloxone in subjects with Alzheimer's disease and age-matched controls. *Biol Psychiatry* 46:412–419. doi:[10.1016/S0006-3223\(98\)00329-1](https://doi.org/10.1016/S0006-3223(98)00329-1)
83. Volpi R, Caffarra P, Marcato A et al (1991) Reduced ACTH/cortisol responses to naloxone in men with Parkinson's disease. *J Neural Transm Park Dis Dement Sect* 3:127–132. doi:[10.1007/BF02260887](https://doi.org/10.1007/BF02260887)
84. Lanzone A, Guido M, Ciampelli M et al (1996) Evidence of a disturbance of the hypothalamic-pituitary-adrenal axis in polycystic ovary syndrome: effect of naloxone. *Clin Endocrinol (Oxf)* 45:73–77. doi:[10.1111/j.1365-2265.1996.tb02062.x](https://doi.org/10.1111/j.1365-2265.1996.tb02062.x)
85. O'Malley SS, Krishnan-Sarin S, Farren C, Sinha R, Kreek MJ (2002) Naltrexone decreases craving and alcohol self-administration in alcohol-dependent subjects and activates the hypothalamo-pituitary-adrenocortical axis. *Psychopharmacology (Berl)* 160:19–29. doi:[10.1007/s002130100919](https://doi.org/10.1007/s002130100919)
86. Delva NJ, Brooks DL, Franklin M et al (2002) Effects of short-term administration of valproate on serotonin-1A and dopamine receptor function in healthy human subjects. *J Psychiatry Neurosci* 27:429–437
87. Invitti C, Danesi L, Dubini A, Cavagnini F (1988) Neuroendocrine effects of chronic administration of sodium valproate in epileptic patients. *Acta Endocrinol (Copenh)* 118:381–388
88. Kritzler RK, Vining EP, Plotnick LP (1983) Sodium valproate and corticotropin suppression in the child treated for seizures. *J Pediatr* 102:142–143. doi:[10.1016/S0022-3476\(83\)80313-8](https://doi.org/10.1016/S0022-3476(83)80313-8)
89. Cavagnini F, Invitti C, Polli EE (1984) Sodium valproate in Cushing's disease. *Lancet* 2(8395):162–163
90. Flück CE, Yaworsky DC, Miller WL (2005) Effects of anti-convulsants on human p450c17 (17alpha-hydroxylase/17,20 lyase) and 3beta-hydroxysteroid dehydrogenase type 2. *Epilepsia* 46:444–448. doi:[10.1111/j.0013-9580.2005.38404.x](https://doi.org/10.1111/j.0013-9580.2005.38404.x)
91. Chappell KA, Markowitz JS, Jackson CW (1999) Is valproate pharmacotherapy associated with polycystic ovaries? *Ann Pharmacother* 33:1211–1216. doi:[10.1345/aph.19096](https://doi.org/10.1345/aph.19096)
92. Beary MD, Lacey JH, Bhat AV (1983) The neuro-endocrine impact of 3-hydroxy-diazepam (temazepam) in women. *Psychopharmacology (Berl)* 79:295–297. doi:[10.1007/BF00433404](https://doi.org/10.1007/BF00433404)
93. Risby ED, Hsiao JK, Golden RN, Potter WZ (1989) Intravenous alprazolam challenge in normal subjects. Biochemical, cardiovascular, and behavioral effects. *Psychopharmacology (Berl)* 99:508–514. doi:[10.1007/BF00589900](https://doi.org/10.1007/BF00589900)
94. Mussig K, Friess E, Wudy SA, Morike K, Haring HU, Overkamp D (2006) Secondary adrenal failure due to long-term treatment with flunitrazepam. *Clin Endocrinol (Oxf)* 65:549–550. doi:[10.1111/j.1365-2265.2006.02622.x](https://doi.org/10.1111/j.1365-2265.2006.02622.x)
95. Risch SC, Janowsky DS, Mott MA et al (1986) Central and peripheral cholinesterase inhibition: effects on anterior pituitary

- and sympathomimetic function. *Psychoneuroendocrinology* 11:221–230. doi:[10.1016/0306-4530\(86\)90057-0](https://doi.org/10.1016/0306-4530(86)90057-0)
96. Peskind ER, Raskind MA, Wingerson D et al (1996) Hypothalamic-pituitary-adrenocortical axis responses to physostigmine: effects of Alzheimer's disease and gender. *Biol Psychiatry* 40:61–68. doi:[10.1016/0006-3223\(95\)00318-5](https://doi.org/10.1016/0006-3223(95)00318-5)
 97. Kumar V, Smith RC, Sherman KA et al (1988) Cortisol responses to cholinergic drugs in Alzheimer's disease. *Int J Clin Pharmacol Ther Toxicol* 26:471–476
 98. Asthana S, Raffaele KC, Greig NH, Schapiro MB, Blackman MR, Soncrant TT (1999) Neuroendocrine responses to intravenous infusion of physostigmine in patients with Alzheimer disease. *Alzheimer Dis Assoc Disord* 13:102–108. doi:[10.1097/00002093-199904000-00008](https://doi.org/10.1097/00002093-199904000-00008)
 99. Rubin RT, O'Toole SM, Rhodes ME, Sekula LK, Czambel RK (1999) Hypothalamo-pituitary-adrenal cortical responses to low-dose physostigmine and arginine vasopressin administration: sex differences between major depressives and matched control subjects. *Psychiatry Res* 89:1–20. doi:[10.1016/S0165-1781\(99\)00085-2](https://doi.org/10.1016/S0165-1781(99)00085-2)
 100. Peskind ER, Raskind MA, Wingerson D et al (1995) Enhanced hypothalamic-pituitary-adrenocortical axis responses to physostigmine in normal aging. *J Gerontol A Biol Sci Med Sci* 50:M114–M120
 101. Rubin RT, Rhodes ME, Miller TH, Jakab RL, Czambel RK (2006) Sequence of pituitary-adrenal cortical hormone responses to low-dose physostigmine administration in young adult women and men. *Life Sci* 79:2260–2268. doi:[10.1016/j.lfs.2006.07.023](https://doi.org/10.1016/j.lfs.2006.07.023)
 102. Laakmann G, Schoen HW, Blaschke D, Wittmann M (1985) Dose-dependent growth hormone, prolactin and cortisol stimulation after i.v. administration of desimipramine in human subjects. *Psychoneuroendocrinology* 10:83–93. doi:[10.1016/0306-4530\(85\)90042-3](https://doi.org/10.1016/0306-4530(85)90042-3)
 103. Nutt D, Middleton H, Franklin M (1987) The neuroendocrine effects of oral imipramine. *Psychoneuroendocrinology* 12:367–375. doi:[10.1016/0306-4530\(87\)90065-5](https://doi.org/10.1016/0306-4530(87)90065-5)
 104. Laakmann G, Wittmann M, Gugath M et al (1984) Effects of psychotropic drugs (desimipramine, chlorimipramine, sulphiride and diazepam) on the human HPA axis. *Psychopharmacology (Berl)* 84:66–70. doi:[10.1007/BF00432027](https://doi.org/10.1007/BF00432027)
 105. Golden RN, Hsiao J, Lane E, Hicks R, Rogers S, Potter WZ (1989) The effects of intravenous clomipramine on neurohormones in normal subjects. *J Clin Endocrinol Metab* 68:632–637
 106. Schule C, Baghai T, Goy J, Bidlingmaier M, Strasburger C, Laakmann G (2002) The influence of mirtazapine on anterior pituitary hormone secretion in healthy male subjects. *Psychopharmacology (Berl)* 163:95–101. doi:[10.1007/s00213-002-1148-5](https://doi.org/10.1007/s00213-002-1148-5)
 107. Schule C, Sighart C, Hennig J, Laakmann G (2006) Mirtazapine inhibits salivary cortisol concentrations in anorexia nervosa. *Prog Neuropsychopharmacol Biol Psychiatry* 30:1015–1019. doi:[10.1016/j.pnpbp.2006.03.023](https://doi.org/10.1016/j.pnpbp.2006.03.023)
 108. Laakmann G, Hennig J, Baghai T, Schule C (2004) Mirtazapine acutely inhibits salivary cortisol concentrations in depressed patients. *Ann N Y Acad Sci* 1032:279–282. doi:[10.1196/annals.1314.038](https://doi.org/10.1196/annals.1314.038)
 109. Lissoni P, Brivio F, Fumagalli L et al (2007) Immune and endocrine mechanisms of advanced cancer-related hypercortisolemia. *In vivo* 21:647–650
 110. Corssmit EP, Heijligenberg R, Endert E, Ackermans MT, Sauerwein HP, Romijn JA (1996) Endocrine and metabolic effects of interferon-alpha in humans. *J Clin Endocrinol Metab* 81:3265–3269. doi:[10.1210/jc.81.9.3265](https://doi.org/10.1210/jc.81.9.3265)
 111. Angioni S, Iori G, Cellini M et al (1992) Acute beta-interferon or thymopentin administration increases plasma growth hormone and cortisol levels in children. *Acta Endocrinol (Copenh)* 127:237–241
 112. de Metz J, Sprangers F, Endert E et al (1999) Interferon-gamma has immunomodulatory effects with minor endocrine and metabolic effects in humans. *J Appl Physiol* 86:517–522
 113. Nolten WE, Goldstein D, Lindstrom M et al (1993) Effects of cytokines on the pituitary-adrenal axis in cancer patients. *J Interferon Res* 13:349–357
 114. Curti BD, Urba WJ, Longo DL et al (1996) Endocrine effects of IL-1 alpha and beta administered in a phase I trial to patients with advanced cancer. *J Immunother Emphasis Tumor Immunol* 19:142–148
 115. Muller H, Hiemke C, Hammes E, Hess G (1992) Sub-acute effects of interferon-alpha 2 on adrenocorticotrophic hormone, cortisol, growth hormone and prolactin in humans. *Psychoneuroendocrinology* 17:459–465. doi:[10.1016/0306-4530\(92\)90004-Q](https://doi.org/10.1016/0306-4530(92)90004-Q)
 116. Spath-Schwalbe E, Hansen K, Schmidt F et al (1998) Acute effects of recombinant human interleukin-6 on endocrine and central nervous sleep functions in healthy men. *J Clin Endocrinol Metab* 83:1573–1579. doi:[10.1210/jc.83.5.1573](https://doi.org/10.1210/jc.83.5.1573)
 117. Lissoni P, Rovelli F, Tisi E et al (1992) Endocrine effects of human recombinant interleukin-3 in cancer patients. *Int J Biol Markers* 7:230–233
 118. Giavoli C, Libé R, Corbetta S et al (2004) Effect of recombinant human growth hormone (GH) replacement on the hypothalamic-pituitary-adrenal axis in adult GH-deficient patients. *J Clin Endocrinol Metab* 89:5397–5401. doi:[10.1210/jc.2004-1114](https://doi.org/10.1210/jc.2004-1114)
 119. Mishra SK, Gupta N, Goswami R (2007) Plasma adrenocorticotropin (ACTH) values and cortisol response to 250 and 1 microg ACTH stimulation in patients with hyperthyroidism before and after carbimazole therapy: case-control comparative study. *J Clin Endocrinol Metab* 92:1693–1696. doi:[10.1210/jc.2006-2090](https://doi.org/10.1210/jc.2006-2090)
 120. Tsatsoulis A, Johnson EO, Kalogera CH, Seferiadis K, Tsolas O (2000) The effect of thyrotoxicosis on adrenocortical reserve. *Eur J Endocrinol* 142:231–235. doi:[10.1530/eje.0.1420231](https://doi.org/10.1530/eje.0.1420231)
 121. Malik KJ, Wakelin K, Dean S, Cove DH, Wood PJ (1996) Cushing's syndrome and hypothalamic-pituitary adrenal axis suppression induced by medroxyprogesterone acetate. *Ann Clin Biochem* 33:187–189
 122. Raedler TJ, Jahn H, Goedecken B, Gescher DM, Kellner M, Wiedemann K (2003) Acute effects of megestrol on the hypothalamic-pituitary-adrenal axis. *Cancer Chemother Pharmacol* 52:482–486. doi:[10.1007/s00280-003-0697-6](https://doi.org/10.1007/s00280-003-0697-6)
 123. Lundgren S, Lonning PE, Utaaker E, Aakvaag A, Kvinnsland S (1990) Influence of progestins on serum hormone levels in postmenopausal women with advanced breast cancer – I. General findings. *J Steroid Biochem* 36:99–104. doi:[10.1016/0022-4731\(90\)90118-C](https://doi.org/10.1016/0022-4731(90)90118-C)
 124. Matin K, Egorin MJ, Ballesteros MF et al (2002) Phase I and pharmacokinetic study of vinblastine and high-dose megestrol acetate. *Cancer Chemother Pharmacol* 50:179–185. doi:[10.1007/s00280-002-0484-9](https://doi.org/10.1007/s00280-002-0484-9)
 125. Chidakel AR, Zweig SB, Schlosser JR, Homel P, Schappert JW, Fleckman AM (2006) High prevalence of adrenal suppression during acute illness in hospitalized patients receiving megestrol acetate. *J Endocrinol Invest* 29:136–140
 126. Leinung MC, Liporace R, Miller CH (1995) Induction of adrenal suppression by megestrol acetate in patients with AIDS. *Ann Intern Med* 122:843–845
 127. Clerico A, Minervini R, Del Chicca MG, Barsantini S, Fiorentini L (1984) Elevated free cortisol plasma levels in patients with prostatic carcinoma undergoing treatment with estrogens. *Int J Clin Pharmacol Res* 4:335–339
 128. Qureshi AC, Bahri A, Breen LA et al (2007) The influence of the route of oestrogen administration on serum levels of cortisol-

- binding globulin and total cortisol. *Clin Endocrinol (Oxf)* 66:632–635. doi:[10.1111/j.1365-2265.2007.02784.x](https://doi.org/10.1111/j.1365-2265.2007.02784.x)
129. Genazzani AR, Lombardi I, Borgioli G et al (2003) Adrenal function under long-term raloxifene administration. *Gynecol Endocrinol* 17:159–168. doi:[10.1080/713603211](https://doi.org/10.1080/713603211)
 130. Späth-Schwalbe E, Piroth L, Pietrowsky R, Born J, Fehm HL (1988) Stimulation of the pituitary adrenocortical system in man by cerulein, a cholecystokinin-8-like peptide. *Clin Physiol Biochem* 6:316–320
 131. Schule C, Baghai T, Sauer N, Laakmann G (2004) Endocrinological effects of high-dose *Hypericum perforatum* extract WS 5570 in healthy subjects. *Neuropsychobiology* 49:58–63. doi:[10.1159/000076411](https://doi.org/10.1159/000076411)
 132. Moro M, Putignano P, Losa M, Invitti C, Maraschini C, Cavagnini F (2000) The desmopressin test in the differential diagnosis between Cushing's disease and pseudo-Cushing states. *J Clin Endocrinol Metab* 85:3569–3574. doi:[10.1210/jc.85.10.3569](https://doi.org/10.1210/jc.85.10.3569)
 133. Schoneshofer M, Fenner A, Altinok G, Dulce HJ (1980) Specific and practicable assessment of urinary free cortisol by combination of automatic high-pressure liquid chromatography and radioimmunoassay. *Clin Chim Acta* 106:63–73. doi:[10.1016/0009-8981\(80\)90375-7](https://doi.org/10.1016/0009-8981(80)90375-7)
 134. Fink RS, Pierre LN, Daley-Yates PT, Richards DH, Gibson A, Honour JW (2002) Hypothalamic-pituitary-adrenal axis function after inhaled corticosteroids: unreliability of urinary free cortisol estimation. *J Clin Endocrinol Metab* 87:4541–4546. doi:[10.1210/jc.2002-020287](https://doi.org/10.1210/jc.2002-020287)
 135. Turpeinen U, Markkanen H, Valimaki M, Stenman UH (1997) Determination of urinary free cortisol by HPLC. *Clin Chem* 43:1386–1391
 136. Findling JW, Pinkstaff SM, Shaker JL, Raff H, Nelson JC (1998) Pseudohypercortisoluria: spurious elevation of urinary cortisol due to carbamazepine. *Endocrinologist* 8:51–54. doi:[10.1097/00019616-199803000-00001](https://doi.org/10.1097/00019616-199803000-00001)
 137. Taylor RL, Machacek D, Singh RJ (2002) Validation of a high-throughput liquid chromatography-tandem mass spectrometry method for urinary cortisol and cortisone. *Clin Chem* 48:1511–1519
 138. Meikle AW, Findling J, Kushnir MM, Rockwood AL, Nelson GJ, Terry AH (2003) Pseudo-Cushing syndrome caused by fenofibrate interference with urinary cortisol assayed by high-performance liquid chromatography. *J Clin Endocrinol Metab* 88:3521–3524. doi:[10.1210/jc.2003-030234](https://doi.org/10.1210/jc.2003-030234)
 139. Schurmeyer TH, Brademann G, von zur Muhlen A (1996) Effect of fenfluramine on episodic ACTH and cortisol secretion. *Clin Endocrinol (Oxf)* 45:39–45. doi:[10.1111/j.1365-2265.1996.tb02058.x](https://doi.org/10.1111/j.1365-2265.1996.tb02058.x)
 140. Razenberg AJ, Elte JW, Rietveld AP, van Zaanen HC, Cabezas MC (2007) A 'smart' type of Cushing's syndrome. *Eur J Endocrinol* 157:779–781. doi:[10.1530/EJE-07-0538](https://doi.org/10.1530/EJE-07-0538)
 141. Lopez AL, Kathol RG, Noyes R Jr (1990) Reduction in urinary free cortisol during benzodiazepine treatment of panic disorder. *Psychoneuroendocrinology* 15:23–28. doi:[10.1016/0306-4530\(90\)90043-9](https://doi.org/10.1016/0306-4530(90)90043-9)
 142. Vicennati V, Ceroni L, Gagliardi L et al (2004) Response of the hypothalamic-pituitary-adrenal axis to small dose arginine-vasopressin and daily urinary free cortisol before and after alprazolam pre-treatment differs in obesity. *J Endocrinol Invest* 27:541–547
 143. Schule C, Baghai T, Rackwitz C, Laakmann G (2003) Influence of mirtazapine on urinary free cortisol excretion in depressed patients. *Psychiatry Res* 120:257–264. doi:[10.1016/S0165-1781\(03\)00204-X](https://doi.org/10.1016/S0165-1781(03)00204-X)
 144. Prinz P, Bailey S, Moe K, Wilkinson C, Scanlan J (2001) Urinary free cortisol and sleep under baseline and stressed conditions in healthy senior women: effects of estrogen replacement therapy. *J Sleep Res* 10:19–26. doi:[10.1046/j.1365-2869.2001.00236.x](https://doi.org/10.1046/j.1365-2869.2001.00236.x)
 145. Ruokonen A, Lund L, Nummi S, Alapiessa U, Viinikka L (1982) Effects of two oral contraceptive combinations, 0.125 mg desogestrel + 0.050 mg ethinylestradiol and 0.125 mg levonorgestrel + 0.050 mg ethinylestradiol on the adrenal function of healthy female volunteers. *Eur J Obstet Gynecol Reprod Biol* 13:259–265. doi:[10.1016/0028-2243\(82\)90107-1](https://doi.org/10.1016/0028-2243(82)90107-1)
 146. MacKenzie MA, Hoefnagels WH, Jansen RW, Benraad TJ, Kloppenborg PW (1990) The influence of glycyrrhetic acid on plasma cortisol and cortisone in healthy young volunteers. *J Clin Endocrinol Metab* 70:1637–1643
 147. Agha A, Monson JP (2007) Modulation of glucocorticoid metabolism by the growth hormone-IGF-1 axis. *Clin Endocrinol (Oxf)* 66:459–465
 148. Ma RC, Chan WB, So WY, Tong PC, Chan JC, Chow CC (2005) Carbamazepine and false positive dexamethasone suppression tests for Cushing's syndrome. *BMJ* 330:299–300. doi:[10.1136/bmj.330.7486.299](https://doi.org/10.1136/bmj.330.7486.299)
 149. Debrunner J, Schmid C, Schneemann M (2002) Falsely positive dexamethasone suppression test in a patient treated with phenytoin to prevent seizures due to nocardia brain abscesses. *Swiss Med Wkly* 132:267
 150. Kyriazopoulou V, Vagenakis AG (1992) Abnormal overnight dexamethasone suppression test in subjects receiving rifampicin therapy. *J Clin Endocrinol Metab* 75:315–317. doi:[10.1210/jc.75.1.315](https://doi.org/10.1210/jc.75.1.315)
 151. Keitner GI, Fruzzetti AE, Miller IW, Norman WH, Brown WA (1989) The effect of anticonvulsants on the dexamethasone suppression test. *Can J Psychiatry* 34:441–443
 152. Putignano P, Kaltsas GA, Satta MA, Grossman AB (1998) The effects of anti-convulsant drugs on adrenal function. *Horm Metab Res* 30:389–397
 153. Roby CA, Anderson GD, Kantor E, Dryer DA, Burstein AH (2000) St John's Wort: effect on CYP3A4 activity. *Clin Pharmacol Ther* 67:451–457. doi:[10.1067/mcp.2000.106793](https://doi.org/10.1067/mcp.2000.106793)
 154. Wenk M, Todesco L, Krahenbuhl S (2004) Effect of St John's wort on the activities of CYP1A2, CYP3A4, CYP2D6, N-acetyltransferase 2, and xanthine oxidase in healthy males and females. *Br J Clin Pharmacol* 57:495–499. doi:[10.1111/j.1365-2125.2003.02049.x](https://doi.org/10.1111/j.1365-2125.2003.02049.x)
 155. Wood PJ, Barth JH, Freedman DB, Perry L, Sheridan B (1997) Evidence for the low dose dexamethasone suppression test to screen for Cushing's syndrome – recommendations for a protocol for biochemistry laboratories. *Ann Clin Biochem* 34:222–229
 156. Charles GA, Orsulak PJ, Rush AJ, Fulton CL (1995) Arecoline reverses dexamethasone suppression of cortisol in normal males: a pilot study. *Biol Psychiatry* 37:811–816. doi:[10.1016/0006-3223\(94\)00215-0](https://doi.org/10.1016/0006-3223(94)00215-0)
 157. Berger M, Doerr P, von Zerssen D (1984) Physostigmine's influence on DST results. *Am J Psychiatry* 141:469–470
 158. Maes M, Van Gastel A, Meltzer HY, Cosyns P, Blockx P, Desnyder R (1996) Acute administration of buspirone increases the escape of hypothalamic-pituitary-adrenal-axis hormones from suppression by dexamethasone in depression. *Psychoneuroendocrinology* 21:67–81. doi:[10.1016/0306-4530\(95\)00028-3](https://doi.org/10.1016/0306-4530(95)00028-3)
 159. Gottfries CG, Nyth AL (1991) Effect of citalopram, a selective 5-HT reuptake blocker, in emotionally disturbed patients with dementia. *Ann N Y Acad Sci* 640:276–279
 160. Bschor T, Baethge C, Adli M et al (2003) Lithium augmentation increases post-dexamethasone cortisol in the dexamethasone suppression test in unipolar major depression. *Depress Anxiety* 17:43–48. doi:[10.1002/da.10078](https://doi.org/10.1002/da.10078)
 161. Kin NM, Nair NP, Amin M et al (1997) The dexamethasone suppression test and treatment outcome in elderly depressed

- patients participating in a placebo-controlled multicenter trial involving moclobemide and nortriptyline. *Biol Psychiatry* 42:925–931. doi:[10.1016/S0006-3223\(97\)00158-3](https://doi.org/10.1016/S0006-3223(97)00158-3)
162. Dommissie CS, Hayes PE, Kwentus JA (1985) Effect of estrogens on the dexamethasone suppression test in nondepressed women. *J Clin Psychopharmacol* 5:315–319
 163. Tiller JW, Maguire KP, Schweitzer I et al (1988) The dexamethasone suppression test: a study in a normal population. *Psychoneuroendocrinology* 13:377–384. doi:[10.1016/0306-4530\(88\)90044-3](https://doi.org/10.1016/0306-4530(88)90044-3)
 164. Gozansky WS, Lynn JS, Laudenslager ML, Kohrt WM (2005) Salivary cortisol determined by enzyme immunoassay is preferable to serum total cortisol for assessment of dynamic hypothalamic–pituitary–adrenal axis activity. *Clin Endocrinol (Oxf)* 63:336–341. doi:[10.1111/j.1365-2265.2005.02349.x](https://doi.org/10.1111/j.1365-2265.2005.02349.x)
 165. Schmid DA, Wichniak A, Uhr M et al (2006) Changes of sleep architecture, spectral composition of sleep EEG, the nocturnal secretion of cortisol, ACTH, GH, prolactin, melatonin, ghrelin, and leptin, and the DEX-CRH test in depressed patients during treatment with mirtazapine. *Neuropsychopharmacology* 31:832–844. doi:[10.1038/sj.npp.1300923](https://doi.org/10.1038/sj.npp.1300923)
 166. Jarrett DB, Pollock B, Miewald JM, Kupfer DJ (1991) Acute effect of intravenous clomipramine upon sleep-related hormone secretion in depressed outpatients and healthy control subjects. *Biol Psychiatry* 29:3–14. doi:[10.1016/0006-3223\(91\)90206-2](https://doi.org/10.1016/0006-3223(91)90206-2)
 167. Skene DJ, Bojkowski CJ, Arendt J (1994) Comparison of the effects of acute fluvoxamine and desipramine administration on melatonin and cortisol production in humans. *Br J Clin Pharmacol* 37:181–186
 168. Steiger A, Benkert O, Holsboer F (1994) Effects of long-term treatment with the MAO-A inhibitor moclobemide on sleep EEG and nocturnal hormonal secretion in normal men. *Neuropsychobiology* 30:101–105
 169. Mann K, Rossbach W, Müller MJ et al (2006) Nocturnal hormone profiles in patients with schizophrenia treated with olanzapine. *Psychoneuroendocrinology* 31:256–264. doi:[10.1016/j.psyneuen.2005.08.005](https://doi.org/10.1016/j.psyneuen.2005.08.005)
 170. Dodt C, Kern W, Fehm HL, Born J (1993) Antimineralocorticoid canrenoate enhances secretory activity of the hypothalamus–pituitary–adrenocortical (HPA) axis in humans. *Neuroendocrinology* 58:570–574
 171. Steiger A, Benkert O, Wöhrmann S, Steinseifer D, Holsboer F (1989) Effects of trimipramine on sleep EEG, penile tumescence and nocturnal hormonal secretion. A long-term study in 3 normal controls. *Neuropsychobiology* 21:71–75
 172. Wiegand M, Berger M (1989) Action of trimipramine on sleep and pituitary hormone secretion. *Drugs* 38(Suppl 1):35–42. discussion 49–50
 173. Sonntag A, Rothe B, Guldner J, Yassouridis A, Holsboer F, Steiger A (1996) Trimipramine and imipramine exert different effects on the sleep EEG and on nocturnal hormone secretion during treatment of major depression. *Depression*. 4:1–13. doi:[10.1002/\(SICI\)1522-7162\(1996\)4:1<1::AID-DEPR1>3.0.CO;2-S](https://doi.org/10.1002/(SICI)1522-7162(1996)4:1<1::AID-DEPR1>3.0.CO;2-S)
 174. Facchinetti F, Volpe A, Farci G et al (1985) Hypothalamus–pituitary–adrenal axis of heroin addicts. *Drug Alcohol Depend* 15:361–366. doi:[10.1016/0376-8716\(85\)90014-6](https://doi.org/10.1016/0376-8716(85)90014-6)
 175. Thakore JH, Barnes C, Joyce J, Medbak S, Dinan TG (1997) Effects of antidepressant treatment on corticotropin-induced cortisol responses in patients with melancholic depression. *Psychiatry Res* 73:27–32. doi:[10.1016/S0165-1781\(97\)00106-6](https://doi.org/10.1016/S0165-1781(97)00106-6)
 176. Hellman L, Yoshida K, Zumoff B, Levin J, Kream J, Fukushima DK (1976) The effect of medroxyprogesterone acetate on the pituitary–adrenal axis. *J Clin Endocrinol Metab* 42:912–917
 177. Leis D, Bottermann P, Ermler R, Henderkott U, Glück H (1980) The influence of high doses of oral medroxyprogesterone acetate on glucose tolerance, serum insulin levels and adrenal response to ACTH. A study of 17 patients under treatment for endometrial cancer. *Arch Gynecol* 230:9–13. doi:[10.1007/BF02108593](https://doi.org/10.1007/BF02108593)
 178. Subramanian S, Goker H, Kanji A, Sweeney H (1997) Clinical adrenal insufficiency in patients receiving megestrol therapy. *Arch Intern Med* 157:1008–1011. doi:[10.1001/archinte.157.9.1008](https://doi.org/10.1001/archinte.157.9.1008)
 179. Giavoli C, Bergamaschi S, Ferrante E et al (2008) Effect of growth hormone deficiency and recombinant hGH (rhGH) replacement on the hypothalamic–pituitary–adrenal axis in children with idiopathic isolated GH deficiency. *Clin Endocrinol (Oxf)* 68:247–251
 180. Trachtenberg J, Zadra J (1988) Steroid synthesis inhibition by ketoconazole: sites of action. *Clin Invest Med* 11:1–5
 181. Albert SG, DeLeon MJ, Silverberg AB (2001) Possible association between high-dose fluconazole and adrenal insufficiency in critically ill patients. *Crit Care Med* 29:668–670. doi:[10.1097/00003246-200103000-00039](https://doi.org/10.1097/00003246-200103000-00039)
 182. Belkien L, Baumann J, Schirpai M, Oelkers W (1983) Propranolol enhances the effect of ACTH on plasma cortisol, but not on aldosterone in man. *J Endocrinol Invest* 6:341–345
 183. Kizildere S, Glück T, Zietz B, Schölmerich J, Straub RH (2003) During a corticotropin-releasing hormone test in healthy subjects, administration of a beta-adrenergic antagonist induced secretion of cortisol and dehydroepiandrosterone sulfate and inhibited secretion of ACTH. *Eur J Endocrinol* 148:45–53. doi:[10.1530/eje.0.1480045](https://doi.org/10.1530/eje.0.1480045)
 184. Ljung T, Ahlberg AC, Holm G et al (2001) Treatment of abnormally obese men with a serotonin reuptake inhibitor: a pilot study. *J Intern Med* 250:219–224. doi:[10.1046/j.1365-2796.2001.00881.x](https://doi.org/10.1046/j.1365-2796.2001.00881.x)
 185. Tomori N, Suda T, Nakagami Y et al (1989) Adrenergic modulation of adrenocorticotropin responses to insulin-induced hypoglycemia and corticotropin-releasing hormone. *J Clin Endocrinol Metab* 68:87–93
 186. Arvat E, Maccagno B, Giordano R et al (2001) Mineralocorticoid receptor blockade by canrenoate increases both spontaneous and stimulated adrenal function in humans. *J Clin Endocrinol Metab* 86:3176–3181. doi:[10.1210/jc.86.7.3176](https://doi.org/10.1210/jc.86.7.3176)
 187. Nishida S, Matsuki M, Adachi N et al (1987) Pituitary–adrenocortical response to metoclopramide in patients with acromegaly and prolactinoma: a clinical evaluation of catecholamine-mediated adrenocorticotropin secretion. *J Clin Endocrinol Metab* 64:995–1001
 188. Gisslinger H, Svoboda T, Clodi M et al (1993) Interferon-alpha stimulates the hypothalamic–pituitary–adrenal axis in vivo and in vitro. *Neuroendocrinology* 57:489–495
 189. Rittmaster RS, Cutler GB Jr, Sobel DO et al (1985) Morphine inhibits the pituitary–adrenal response to ovine corticotropin-releasing hormone in normal subjects. *J Clin Endocrinol Metab* 60:891–895
 190. Allolio B, Schulte HM, Deuss U, Kallabis D, Hamel E, Winkelmann W (1987) Effect of oral morphine and naloxone on pituitary–adrenal response in man induced by human corticotropin-releasing hormone. *Acta Endocrinol (Copenh)* 114:509–514
 191. Michelson D, Galliven E, Hill L, Demitrack M, Chrousos G, Gold P (1997) Chronic imipramine is associated with diminished hypothalamic–pituitary–adrenal axis responsiveness in healthy humans. *Clin Endocrinol Metab* 82:2601–2606. doi:[10.1210/jc.82.8.2601](https://doi.org/10.1210/jc.82.8.2601)
 192. Korbonits M, Trainer PJ, Edwards R, Besser GM, Grossman AB (1995) Benzodiazepines attenuate the pituitary–adrenal responses to corticotrophin-releasing hormone in healthy volunteers, but not in patients with Cushing’s syndrome. *Clin Endocrinol (Oxf)* 43:29–35