REVIEW

Acta Neurobiol Exp 2018, 78: 187–197
DOI: 10.21307/ane-2018-017

Role of food-drug interactions in neurological and psychological diseases

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Given that foods and nutrients have been shown to influence the pharmacokinetics of drugs, drugs may cause changes in the nutritional status of patients and their response to a given drug. Food-drug interactions are particularly relevant for drugs used to treat neurological and psychological diseases. This review provides an overview of food-drug interaction in the treatment of neurological and psychological diseases. A literature search was carried out by collecting data from different reviews, reports, and original articles on general or specific drug interactions with food, in patients with a variety of neurological and psychological diseases. Based on our review, we found that food-drug interactions may alter the expected impact of drug, or cause the development of a drug toxicity. Nutritional status of the patients may also be affected, particularly a change in body weight caused by a change appetite. Metabolism, absorption, and excretion of foods may also be altered, and nutritional insufficiencies may occur. Recent studies show that diet can have a strong influence on gut microbiota and thus, alter drug pharmacokinetics. Therefore, microbiota alterations should also be considered while assessing food-drug interactions. Knowledge of food-drug interactions is critical for improving health of patients with neurological and psychological diseases, and also for improving effectiveness of treatments.

Key words: neurological diseases, psychological diseases, food-drug interaction

INTRODUCTION

Various drugs are used in the treatment of acute and chronic diseases. However, it is important to take the drugs safely and effectively during therapy. Although concerns about drug-drug interactions frequently come to mind, interactions may also occur between drugs and foods, particularly with plants. However, studies on food-drug interactions are more limited than those on drug-drug interactions (Bushra et al. 2011, Otles and Senturk 2014). A food-drug interaction is the consequence of a physical, chemical, or physiologic relationship between a drug and a product consumed as food or a nutrient present in a botanically-derived food or dietary supplement. The influence of dietary substances on drug effects depends on numerous variables, including physicochemical properties of the drug, and enzymes and transporters present in the gastrointestinal tract. Food-drug interactions may affect pharmacokinetic and pharmacodynamic properties of drugs (Choi and Ko 2017).

Food-drug interactions are particularly relevant for neurological and psychological diseases. In general, neurological or psychological diseases involve the brain, brainstem, spinal cord or peripheral nervous system disorders, as well as systemic disorders of the muscles (Aksoy 2016). Depression, schizophrenia, Parkinson's disease, Alzheimer's, epilepsy, bipolar disorder, general anxiety disorder, and sleep problems are all included in this disease group. Common drug classes used to treat these conditions include anticonvulsants for epilepsy, antipsychotic drugs for schizophrenia, dopaminergic agents for Parkinson's, and an-

Received 11 October 2017, accepted 19 June 2018

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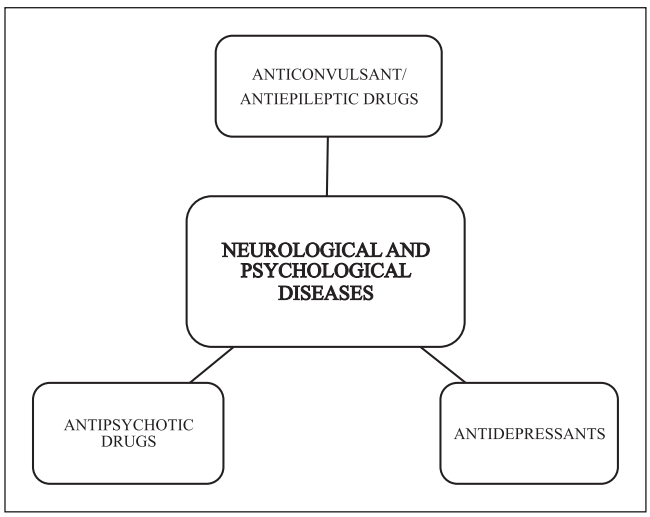

Fig. 1. Main classes of drugs used to treat neurological and psychological diseases (e.g. depression, Parkinson's disease, schizophrenia).

tidepressants for depression as well as panic attacks. In each drug group, different food-drug interactions may occur. Awareness of interactions with these drugs is important in terms for the health of the patients as well as the effectiveness of the treatment (WHO 2006, Otles and Senturk 2014, FDA 2016). To examine this, the present review is focused on providing an overview of interactions of the main drug groups used in neurological and psychological diseases (Fig. 1) with food/nutrients, and impacts of the drugs on body weight and appetite.

A literature research was carried out by collecting recent data from different reviews, reports, and original articles on general or specific drug interactions with food in neurological and psychological diseases.

ANTICONVULSANT/ANTIEPILEPTIC DRUGS

Anticonvulsant drugs are commonly used in the treatment of epilepsy, and are used to control seizures. The main purpose of anticonvulsant treatment is to reduce brain damage by preventing the onset of seizures (Aksoy 2016, Kirmani et al. 2016).

Common anticonvulsant drugs include phenytoin, barbiturates i.e phenobarbital, primidone, carbamazepine, sodium valporate (VPA), felbamate, topiramate, and zonisamide. There are many studies showing that these drugs interact with food and nutrients (Arslan et al. 2009, Hosseinpour et al. 2007, Lee and Yu 2015).

The anticonvulsant drugs, particularly phenytoin, barbiturates, carbamazepine, and VPA, may cause vitamin D deficiency by increasing vitamin D metabolism in the liver. Vitamin D deficiency may cause calcium absorption in the small intestine to deteriorate, an increase in calcium extraction from the bones, and a reduction in bone mineral density. Chronic anticonvulsant drug use may cause bone loss and osteomalacia in adults, and rickets in children (Baek et al. 2014, Başoğlu et al. 1999, Hosseinpour et al. 2007, Vestergaard 2015). In a study of children with epilepsy who receive anticonvulsant treatment, there was a negative correlation between plasma 25 hydroxy vitamin D levels and drug use, such that 82.5% of children developed a new vitamin D deficiency after initiation of treatment (Lee and Yu 2015). Similarly, in a separate study of children with epilepsy on long-term (>1 year) antiepileptic drugs, 55 Malaysian children (22.5%) had vitamin D deficiency and another 48 (19.7%) had vitamin D insufficiency. Polytherapy (>1), age (>12 years old), sun exposure time (30–60 min/day or <30 min/day) were identified as significant risk factors for vitamin D deficiency (Fong et al. 2016).

Anticonvulsant drugs may compete with biotin in the human intestine, and inhibit the transport of biotin by influencing the substrate transport system in the enterocyte brush border membrane layer. In addition, anticonvulsant drugs may increase the excretion of biotin by accelerating biotin catabolism and metabolism which may cause biotin deficiency, as well as lower serum and liver biotinides activity (Arslan et al. 2009, Mock et al. 1998, Pronsky and Crowe 2012, Rathman et al. 2003). In a study of rats receiving carbamazepine treatment, supplementation with 0.06 g/kg biotin was associated with a reduction in plasma free biotin, and pyruvate carboxylase and acetyl CoA carboxylase enzyme activity. Supplementation with 6 mg/kg biotin was associated with an increase in free biotin, and a prevention of the reduction in decrease in pyruvate and acetyl CoA carboxylase enzyme activity. Also the biotin supplementation showed positive effect (Arslan et al. 2009).

Several studies have demonstrated that an increase in serum homocysteine levels among patients receiving anticonvulsant treatment may cause a deficiency in folic acid, vitamin B_6, and vitamin B_{12}, which may, in turn, increase risk for cardiovascular diseases (Karabiber et al. 2003, Sener et al. 2006). The type of anticonvulsant drug used is effective at modulating homocysteine, B_{12}, and folic acid levels. In particular, there was no difference between homocysteine, B_{12}, and folic acid levels in oxcarbazepine-treated epilepsy patients compared to controls (Rezaei et al. 2017). However, meta-analyses show that homocysteine levels are significantly higher among patients receiving carbamazepine and sodium VPA relative to control, whereas serum folate levels are significantly lower in patients receiving carbamazepine compared to controls. On the other hand, carbamazepine treatment is associated with a reduc-

tion in serum folate levels, and treatment with sodium valproate is associated with a reduction in serum vitamin B_{12} levels (Gorjipour et al. 2013, Ni et al. 2014). The patient group treated with VPA group had higher serum levels of homocysteine compared to the control group (Ni et al. 2014). In addition, patients receiving VPA had significantly lower serum folate levels relative to controls (Bächle et al. 2015).

Several studies have examined methylenetetrahydrofolate reductase (MTHFR) gene polymorphism and homocysteine levels among epileptic patients receiving antiepileptic drug treatment (Di Rosa et al. 2013, Munisamy et al. 2015, Semmler et al. 2013). A difference in the methylation levels of MTHFR amplicon was observed between antiepileptic drug-treated patients with epilepsy and controls. There was also a positive correlation between serum folate levels and peripheral blood MTHFR amplicon methylation status. Thus, antiepileptic drug monotherapy may affect one carbon metabolism, which may subsequently lead to hypo-methylation in certain regions of deoxyribonucleic acid (Bächle et al. 2015). Munisamy et al. (2015) found a significant increase in mean homocysteine levels in epileptic patients receiving anti-epileptic drug monotherapy (i.e. phenytoin carbamazepine or VPA), as well as a reduction in mean folic acid and vitamin B_{12} among toxicity and non-toxicity groups. For patients with epilepsy who also had the MTHFR C677T polymorphism, particularly those with the TT genotype, homocysteine levels were higher and folic acid and B_{12} levels were lower compared to control groups (Munisamy et al. 2015). Di Rosa et al. 92013) found higher homocysteine levels in patients with MTHFR polymorphism. In contrast, results of a study of 498 antiepileptic drug-treated epilepsy patients by Semmler et al. (2013) suggest that folate and vitamin B_{12} play important roles in the development of hyper-homocysteinemia. Importantly, in that study, there was no relationship between genes and risk of developing hyper-homocysteinemia during antiepileptic drug treatment. Given these results, subsequent studies have investigated the effects of vitamin supplement on homocysteine levels (e.g. Bochyńska et al. 2012, Chandrasekaran et al. 2017). One study examined the effects of 0.4 mg/day folate, 50 mg/day vitamin B_6, and 100 mcg/day vitamin B_{12} supplementation among patients receiving Carbamazepine and VPA treatment. After one year of supplementation, the authors observed a significant decline in the Beck Depression Inventory, in the hyper homocysteinemia, and in seizure frequency observed (Bochyńska et al. 2012). In another study of children receiving carbamazepine and phenytoin treatment, supplementation with 5 mg/day folic acid for one month was associated with an increase in serum homocysteine levels, and a reduction in B_{12} and folic acid levels (Chandrasekaran et al. 2017). Supplementation was also associated with a reduction in plasma homocysteine concentrations in the study group (Chandrasekaran et al. 2017). Given these results levels of vitamin $B_{6,}$ vitamin B_{12}, and folic acid should be monitored among patients receiving anticonvulsant drugs, and supplementation may be beneficial (Bochyńska et al. 2012, Chandrasekaran et al. 2017). On the other hand, excess intake of folic acid may reduce the effectiveness of the drug. In a case study, it was demonstrated that 5 mg/day folic acid supplementation was associated with a reduction in serum phenytoin concentration, and an increase in number of seizure attacks (Seligmann et al. 1998). Phenytoin and phenobarbital may also affect vitamin K metabolism, leading to deficiency (Elmacioğlu 2007).

VPA is a drug that is routinely used during epilepsy attacks. VPA administration may cause carnitine deficiency by reducing endogenous carnitine synthesis via enzyme inhibition, inhibition of the intracellular carnitine transport, and/or by reducing absorption of free carnitine and acyl-carnitine (Bykov et al. 2004, Moreno et al. 2005, Wu et al. 2004). Carnitine deficiency was found in approximately 17% of patients with epilepsy and was significantly associated with carnitine-free enteral formula only by tube feeding (Fukuda et al. 2015). At the same time, plasma VPA concentrations were slightly higher in carnitine deficient rats than in controls (Katayama et al. 2016). In one study of schizophrenic patients receiving VPA treatment, supplementation of 30 mg/kg levo-carnitine supplementation was associated with an increase in serum carnitine levels relative to baseline (Nakamura and Nagamine 2015). This increase was accompanied by a general recovery in mental status. Based on these results, the authors suggest that carnitine supplementation may be beneficial among schizophrenic patients receiving VPA (Nakamura and Nagamine 2015). Other studies have shown that VPA is influenced by high fat intake. For example, in one study, rats were given a die that included high fructose (45% fructose) as well as high fat diet (20% fat) for 30 days. Animals receiving the high fat and fructose diets, as well as VTA, demonstrated deregulated lipid metabolism, loss of insulin sensitivity, increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, enhanced CYP2E1 activity and oxidative damage, and reduced cellular antioxidants (Sathiya Priya et al. 2016). Moreover, a study of patients receiving VPA treatment linked a high-fat diet (77.5% fat) with increased hepatotoxicity, via modulation of mitochondrial β-oxidation. Based on these results, some authors have suggested that patients on VPA should avoid a high-fat diet (Zhang et al. 2014).

Another problem that may be observed during VPA treatment is hypocalcemia. Although hypocalcemia is also observed following phenytoin treatment, this effect is thought to be caused by phenytoin's inhibition of vitamin D hydroxylation. VPA, on the other hand, it thought to affect calcium via a pathway that is separate from vitamin D. It has been proposed that metabolites of VPA cause hypocalcemia by binding with calcium (Davison et al. 2011).

In addition to changes in calcium, long-term VPA treatment may cause a reduction in serum levels of zinc, hair zinc and copper levels (Armutcu et al. 2004, Yilmaz et al. 2009). However, one study suggested that, even if serum zinc levels were low or normal among patients treated with VPA, the drug did not significantly affect activity of serum zinc, biotin, and biotinidase (Castro-Gago et al. 2011).

VPA has also been shown to interact with soybeans. In one study, rats were pretreated with either 150 mg/kg or 500 mg/kg of soy extract for five days. VPA C_{max} values were decreased to 57% for those pretreated with 150 mg soy, and to 65% for those treated with 500 mg. Of note, gamma aminobutyric acid (GABA) concentrations in the brain were increased within 5 min after VPA injection. In the soy-treated group, concentrations of GABA in the brain were significantly inhibited throughout the entire study period; however, plasma levels of GABA were not significantly different between the treatment and control groups (Marahatta et al. 2014).

Anticonvulsant drugs were associated with levels of trace elements. In a study conducted in 307 patients with epilepsy receiving treatment with either conventional or newer antiepileptic drugs and 42 controls, it was found that trace element status was significantly altered among both patient groups compared to the control group. Compared to controls, patients receiving levetiracetam had higher zinc, selenium, copper, iron, aluminum, cadmium, cobalt, and nickel levels, whereas levels of manganese and lead did not differ between groups. Similar elevations in metals were observed in other monotherapy groups, except for levels of nickel, iron, lead, and selenium (Sarangi et al. 2014).

Anticonvulsant drugs can also impact on body weight. Felbamate, topiramate and zonisamide are associated with a decrease in body weight. Phenytoin does not have impact on body weight, whereas gabapentin, pregabalin, carbamazepine and VPA may increase body weight by increasing appetite (Antel and Hebebrand 2012, Ben-Menachem 2007, Pronsky and Crowe 2012). One study found that the increase in bodyweight among patients taking VPA may be caused by a decrease in serum glucose levels, an increased desire to eat, increased energy intake, fasting, overeating, depression, and increased glucagon-like peptide-1 (Martin et al. 2009).

Anticonvulsant drugs can also interact with alcohol by altering the metabolism or effects of alcohol and/or the drug. Some of these interactions can occur even at moderate drinking levels and cause adverse health effects for the drinkers. Thus, it is suggested to avoid taking anticonvulsant drugs with alcohol (Vernon 2013).

DOPAMINERGIC AGENTS

Levodopa 3–4 dihydroxy phenyl alanine is the precursor of dopamine and is used in pharmacological treatment of Parkinson's disease (PD). Dopaminergic agents used in treatment can precursors of dopamine with decarboxylase inhibitor carbidopa/levodopa, dopamine agonists, bromocriptine, and pergolide (Akbulut 2009).

Methylation of levadopa is catalyzed by catechol-O-methyltransferase, which drives the production of S-adenosyl homocysteine. Levadopa can be reversibly hydrolyzed to homocysteine. Folate, vitamin B_6, and vitamin B_{12} are all cofactors for the production of homocysteine enzymes, and deficiencies in any one of these can lead to elevated homocysteine (Qureshi et al. 2008, Rozycka et al. 2013). At the same time, a polymorphism in the MTHFR and methylenetetrahydrofolate dehydrogenase 1 (MTHFD1) genes affecting folate and homocysteine metabolism may enhance the effect of levodopa on homocysteine among PD patients, and cause an additional elevation in concentration of homocysteine (Oliveira et al. 2017, Rozycka et al. 2013). High concentrations of homocysteine in PD may have detrimental effects on dopaminergic neurons (Rozycka et al. 2013). One study reported significantly higher levels of homocysteine among PD patients receiving levodopa treatment. Further, patients with PD had higher aortic strain and aortic stiffness index, which were correlated with higher serum homocysteine levels. Among PD patients, there was also a negative correlation between aortic distensibility and serum homocysteine levels (Günaydın et al. 2016). In a study conducted on 60 PD and 82 healthy subjects treated with levodopa, PD patients were more likely to show the MTHFR TT677 gene polymorphism and higher homocysteine levels compared to controls. At the same time, total coenzyme Q10 (CoQ10) was significantly lower in PD patients than in healthy subjects, and as consequence, percent content of oxidized versus total CoQ10 was higher in the patient group compared to controls. PD patients with the TT677 polymorphism exhibited the highest levels of homocysteine and percent content of oxidized versus total CoQ10. TT677 genotype and levodopa daily dose

were independently and directly correlated with levels of homocysteine and CoQ10 (Gorgone et al. 2012). One recent meta-analysis summarized results of 15 studies in which plasma homocysteine B_{12} and folate levels and cognitive function were assessed in PD patients, who were divided into two groups: those with cognitive impairment (PDCI) and those without cognitive impairment (PDNC). Results of the meta-analysis demonstrate that, overall, homocysteine concentration is higher among PD patients than among healthy controls. Within PD patients, there were significant differences between PDCI and PDCN groups for homocysteine, vitamin B_{12}, and folate. In particular, levels of homocysteine were higher, and levels of vitamin B_{12} and folate were lower among PDCI patients compared to PDCN patients (Xie et al. 2017). Therefore, adequate intake of folate, vitamin B_6 and vitamin B_{12} in diet may reduce the impact of levodopa by preventing an increase in homocysteine levels (Qureshi et al. 2008).

Intake of levodopa with foods, the time of ingestion of a meal, fat, fiber, ascorbic acid may change the effectiveness of drug in the body (Fernandez et al. 2010). Patients receiving levodopa treatment should be monitored for food intake with the drug, carbohydrate and protein content of the meals, and associated micronutrient deficiencies. Patient diets should be regulated in accordance with the meal that the drug is taken (Akbulut 2009, Ismail 2009). Absorption rate of levodopa may increase during fasting and its absorption may decrease or delay as a result of its intake with particular foods (Akbulut 2009). Nutritional content of the meals also has an impact on levodopa. In particular, protein may inhibit the absorption of levodopa by modulating gastric discharge time and the transport mechanism of the drug. At the same time, the neutral amino acids (e.g. valine, isoleucine, tryptophan, phenylalanine, tyrosine) may prevent levodopa from crossing the blood brain barrier by competing with the drug. Thus, levodopa should not be taken in conjunction with a high-protein diet (Akbulut 2009, Aksoy 2016, Ismail 2009). Moreover, high carbohydrate intake causes an increase in insulin secretion which may cause a reduction in the neutral amino acids, and in turn, cause an increase in effectiveness levodopa (Akbulut 2009). One study examined a group of PD patients taking amino acid supplements 60 minutes after lunch and 60 minutes after dinner (for a total daily dose of 16 g) each time at least 60 minutes before the following levodopa administration for six months. The control group received placebo according to the same procedure. The authors observed a significant increase in mini-nutritional assessment scores in the group receiving both amino acid supplements and levodopa treatment. In both groups, there was a decrease in Quantitative Insulin Sensitivity Index after six months. After six months of supplementation, there were no changes in low-density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol levels. However, oxidized glutathione levels decreased by 28% over time in the intervention group, but increased by 55% in the placebo (Cucca et al. 2015).

In one study, administration of a banana juice (a mixture of fresh banana and water) was associated with reduced bioavailability of levodopa by drug-food interaction in rats. In particular, banana juice was associated with a significant decrease in C_{max} of levodopa. Interestingly, however, administration of levodopa with a commercial beverage containing 10% banana juice resulted in no significant change in C_{max}. Based on these results, the authors concluded that patients should be advised against mixing levodopa and fresh banana juice (Ogo et al. 2005).

Besides the impact of foods on levodopa, this drug may also cause specific nutritional deficiencies. Indeed, nutritional deficiencies are frequently reported among patients with PD. Administration of levodopa and carbidopa may create a deficiency by inhibiting the kynurenine hydrolase enzyme that takes part in oxidative way of the tryptophan, and subsequently prevent the synthesis of niacin (Bender et al. 1979).

ANTIDEPRESSANTS

Psychotropic drugs are a large group of medications that affect the nervous system through different mechanisms. Patients with depression and bipolar disorder are treated with a variety of psycho-pharmaceuticals. Among these pharmaceuticals are antidepressants, such as selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants and a variety of antipsychotic drugs (Ornoy et al. 2017, Yohn et al. 2017).

Selective Serotonin Reuptake Inhibitors (SSRIs)

SSRIs inhibit serotonin reuptake in raphe nuclei neurons, and chronic treatment results in an increase in serotonin levels throughout the brain (Yohn et al. 2017). Fluoxetine is one of the most frequently prescribed SSRIs. In one study of patients receiving fluoxetine treatment, hypoglycemia was observed 72 hours after taking the drug, likely due to an increase in blood insulin levels (Deeg and Lipkin 1996). In another study, there was significant reduction in bodyweight and visceral adipose tissue after 12 weeks

of fluoxetine treatment (Aggarwal et al. 2016). A review reported that SSRIs affected bodyweight in the short term, but not the long term (Reekie et al. 2015). However, the effects of SSRIs on body weight may not be uniform across individuals. Given the importance of adequate nutrition in early life, there may be long-term effects of early malnutrition on development of the serotoninergic system. For example, one study showed a reduction in food intake and weight gain with chronic treatment of citalopram among well-nourished rats, but not in early malnourished rats even in their adult stage (Barreto Medeiros et al. 2002). On the other hand, a case report demonstrated that SSRI treatment could be beneficial to control episodes of nocturnal eating/drinking disorder, potentially by improving sleep habits (Miyaoka et al. 2003). Moreover, SSRI treatment combined with aspirins or anti-nonsteroidal anti-inflammatory drugs have been shown to risk of increase upper gastrointestinal bleeding (Jiang et al. 2015, Yuan et al. 2006), which potentiality alters food intake – particularly among the elderly.

Sertraline and Paroxetine have been linked to higher LDL cholesterol, and long-term treatment may increase risk of cardiovascular disease (Wei et al. 2009).

At the same time, a reduction of serum copper level by 14% has been reported among patients receiving citalopram treatment (Schlegel-Zawadzka and Nowak 2000).

Monoamine Oxidase Inhibitors (MAOIs)

The earliest drugs found to successfully treat depression were MAOIs. MAOIs inhibit the oxidation of monoamines and ultimately result in increased extracellular levels of serotonin, norepinephrine, and dopamine throughout the brain (Yohn et al. 2017). Although MAOIs are very effective in treatment of the depressive diseases, studies have reported adverse effects such as hypertensive attacks, as a result of a drug interaction with foods containing tyramine (Pronsky and Crowe 2012, Volz and Gleiter 1998). Tyramine is a sympathomimetic agent that has an indirect impact on blood pressure when ingested concurrently with an MAOI. In the presence of an MAOI, tyramine digestion cannot occur and the tyramine participates in the circulation is taken by adrenergic neurons and causes a hypertensive attack (Flockhart 2012). For this reason, consumption of food containing tyramine should be avoided (Aksoy 2016, Pronsky and Crowe 2012).

The MAOI phenelzine may cause a deficiency, by also creating pyridoxal hydrazine without enzymatic effect and preventing vitamin B_6 from turning into an active form (Aksoy 2016). One study found that the active form of vitamin B_6 pyridoxal phosphate decreased by a rate of 54% among patients receiving phenelzine (Malcolm et al. 1994).

The MAOIs in the hydrazine class, including phenelzine and isocarboxazide, may cause hypoglycemia and an increase in body weight (McIntyre et al. 2006, Pronsky and Crowe 2012). These effects may occur via an increase in serotonin that increases the amount of glucose entering the brain, and/or increasing the glucose excretion rate. The net effect is a reduction in blood glucose levels, which may cause an increase in bodyweight by increasing appetite and changing the energy balance (Pronsky and Crowe 2012, Ruetsch et al. 2005).

Tricyclic Antidepressants (TCAs)

TCAs were developed in the mid-1950s, with proven effectiveness, and are used in the treatment of major depression. TCAs affect the serotonergic and noradrenergic systems by blocking the serotonin and norepinephrine transporters (Ornoy et al.2017, Yohn et al. 2017). The TCA group includes: amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, and protriptyline (Ornoy et al. 2017).

High dietary fiber intake may decrease absorption of the TCA amitriptyline, thereby decreasing the drug's activity (Pronsky and Crowe 2012). Therefore, consumption of high fiber foods, including legumes, fish, meat, and vitamin C-rich foods, may cause a decrease in the absorption of amitriptyline (Ismail 2009).

TCAs may also cause a decrease in the plasma tryptophan concentration and an increase in the concentration of tryptophan in the brain (Eriksson and Walinder 1998). Low plasma tryptophan values have been observed after only six months after treatment (Fekkes et al. 1997).

TCAs, especially amitriptyline, may cause increasing in body weight by stimulating hunger, increasing carbohydrate consumption, and by influencing the energy balance (Ruetsch et al. 2005). These effects may vary depend on the dosage of the drug.

ANTIPSYCHOTIC DRUGS

Antipsychotic drugs are used for the treatment of psychosis, depression, anxiety, bipolar disorders and obsessive-compulsive disorders. They affect the brain by blocking dopamine receptors and reducing dopamine effects. Antipsychotic drugs are divided into first (i.e. typical) and second (i.e. atypical) genera-

tion. Typical antipsychotics include: chlorpromazine, fluphenazine, haloperidol, loxapine, perphenazine, pimozide, thioridazine, thiothixene, trifluoperazine, and triflupromazine. The atypical antipsychotics include: aripiprazole, clozapine, olanzapine, quetiapine, and ziprasidone (Ornoy et al. 2017).

Antipsychotic drugs may cause an increase in appetite without affecting energy consumption, and may thus cause an increase in body weight (Aksoy 2016, Pronsky and Crowe 2012, Reekie et al. 2015). In one study, clozapine treatment for at least one year was associated with an increase in body mass index (BMI), and the increase in BMI was higher among patients with the polymorphisms in the leptin gene and 5-hydroxytryptamine receptor 2C (HTR2C) gene (Kang et al. 2014).

One study documented a significant increase in BMI after 13 weeks of oral risperidone or flupenthixol treatment (Emsley et al. 2015). However, after antipsychotic treatment for 16 weeks, the mean change in BMI was -1.9% for the intervention group and +0.6% for the control group. Further, the difference in BMI from baseline was associated with duration of illness and a metabolic risk index, suggesting that healthy nutrition and physical activity may be effective in controlling body weight during treatment (Magni et al. 2017).

Second generation antipsychotics have been shown to influence blood glucose and lipids (Aksoy 2016). In a study carried out on obese schizophrenic patients receiving clozapine treatment, serum triglyceride and total cholesterol/high-density lipoprotein (HDL) cholesterol levels were higher than observed in a control group who did not receive the drug treatment. In addition, those taking clozapine showed a higher high homeostatic model assessment (HOMA) index and lower insulin sensitivity, compared to controls (Wu et al. 2008). The observed effect of clozapine on blood glucose may derives from its negative impact on the pancreas, and may cause hyperglycemia by modulating glucose metabolism. Blood glucose levels appear to be increased most dramatically by the antipsychotic clozapine, followed by olanzapine, quetiapine, risperidone and ziprasidone. These drugs may also cause an increase in risk of cardiovascular disease by influencing triglyceride, HDL cholesterol, and low-density lipoprotein (LDL) cholesterol (Aksoy 2016).

Antipsychotic drugs can also interact with micronutrients. The antipsychotic chlorpromazine thorozin has been shown to increase riboflavin excretion and may therefore cause riboflavin deficiency. Chloropromazine thorozin may also cause vitamin B_{12} deficiency (Elmacioğlu 2007, Pronsky and Crowe 2012). Another study found that serum levels of the antipsychotic fluphenazine (permitil, prolixin) decreased by 25% when taken with ascorbic acid supplementation (Dysken et al. 1979).

Constipation is a recognized side effect of the second generation antipsychotic clozapine, depending on the movements of the smooth muscle in the intestinal wall. Therefore, patients taking clozapine should maintain sufficient water and fiber intake (Elmacioğlu 2007).

While ziprasidone should be taken with foods, the other drugs should be taken on an empty stomach. In addition, it is necessary to avoid alcohol and caffeine use with antipsychotic drugs (Food and Drug Administration 2016).

SLEEPING PILLS

Sleeping pills ease sleeping problems by decelerating brain activity. They are used to treat problems in falling or staying asleep. Eszopiclane and zolpidem are examples of sleeping pills (Food and Drug Administration 2016).

Patients should avoid taking sleeping pills with alcohol. When taken with caffeine, sleeping pills may increase anxiety, and the effectiveness of the sleeping pills may decrease (Food and Drug Administration 2016, Ismail 2009).

According to the US Food and Drug Administration (FDA), sleeping pills should not be taken with a meal or immediately after a meal (FDA 2016). Indeed, one study found lower plasma zolpidem levels 20 minutes to 3 hours following a dose in those receiving a high fat diet compared to a fasted state. After four hours, however, those on the high fat diet demonstrated higher plasma zolpidem levels (Greenblatt et al. 2013). Further, studies have reported an interaction between zolpidem and St John's wort (SJW). In one study, fourteen healthy male subjects received a single 10 mg oral dose of zolpidem followed by 300 mg orally, three times a day of SJW, for 14 days. After repeated administration of SJW, there was a reduction in mean values of C_{max} for zolpidem. This effect SJW on the pharmacokinetics of zolpidem has not previously been reported. Repeated administration of SJW decreased the plasma concentration of zolpidem, potentially by enhancing CYP3A4 activity (Hojo et al. 2011).

Triazolam, another drug used to treat insomnia, has been shown to interact with grapefruit juice. Hukkinen et al. (1995) demonstrated that triazolam taken with 250 ml of grapefruit juice resulted in an increase in peak concentration of the drug, as well as an increase in drowsiness (Hukkinen et al. 1995).

The aforementioned food-drug interactions in neurological and psychological diseases are summarized in Table I.

Table I. Summary of food-drug interactions in neurological and psychological diseases.

Drugs	Effects and Considerations	References
Anticonvulsant/Antiepileptic Drugs	They may cause hyper-homosisteinemia due to the folic acid, vitamin B_6, vitamin B_{12} deficiency and MTHFR gene polymorphism.	Rezaei et al. 2017 Bächle et al. 2015 Munisamy et al. 2015
	The use of anticonvulsant drugs with alcohol should be avoided.	Vernon 2013
Phenytoin, barbiturates, carbamazepine, VPA	They may cause vitamin D deficiency and deteriorate calcium absorption.	Baek et al. 2014 Hosseinpour et al. 2007 Vestergaard 2015
	They may cause biotin deficiency, low serum and liver biotinides activity.	Arslan et al. 2009 Pronsky and Crowe 2012 Rathman et al. 2003
VPA	It may cause carnitine deficiency by reducing endogenous carnitine synthesis.	Fukuda et al. 2015 Katayama et al. 2016
	It may cause hypocalcemia.	Davison et al. 2011
	It may reduce the serum and hair zinc.	Armutcu et al. 2004 Yilmaz et al. 2009 Castro-Gago et al. 2011
	High-fat diet and soy intake with drug should be avoided.	Zhang et al. 2014 Marahatta et al. 2014
Gabapentin, pregabalin, carbamazepine and VPA	They may increase body weight by increasing appetite.	Antel and Hebebrand 2012 Ben-Menachem 2007 Pronsky and Crowe 2012 Martin et al. 2009
Levodopa	If patients has vitamin B_6 and vitamin B_{12} deficiency or polymorphism in *MTHFR* and *MTHFD1* genes, drugs may cause hyperhomocystenaemia.	Xie et al. 2017 Oliveira et al. 2017
	High protein intake may prevent levodopa to cross blood brain barrier.	Aksoy 2016 Ismail 2009
Selective Serotonin Reuptake Inhibitors (SSRI)		
Fluoxetine	It may cause weight loss and decreasing visceral adipose tissue.	Aggarwal et al. 2016
Sertraline and paroxetine	They was related to high LDL- cholesterol, and in the long-term treatment it might pose a risk to cardiovascular disease.	Wei et al. 2009
Citalopram	Serum copper levels may reduce in drug users.	Schlegel-Zawadzka and Nowak 2000
Monoamine Oxidase Inhibitors (MAOIs)	It is necessary to avoid consumption of these foods with MAOIs.	Flockhart 2012 Aksoy 2016 Pronsky and Crowe 2012
Phenelzine	The drug may prevent vitamin B_6 to turn into active form.	Malcolm et al. 1994
Phenelzine and isocarboxazide	Increasing in body weight. The drugs may increase the appetite. They may change the energy balance.	McIntyre et al. 2006 Pronsky and Crowe 2012 Ruetsch et al. 2005
Tricyclic Antidepressants (TCAs)	Dietary high fiber, legume, fish, meat and vitamin C-rich foods intake may cause a decrease in the absorption of the TCA.	Pronsky and Crowe 2012 Ismail 2009
	It may decrease in the plasma tryptophan concentration and an increase in the concentration of tryptophan in the brain.	Eriksson and Walinder 1998 Fekkes et al. 1997
	It may increase body weight by stimulating hunger and increasing carbohydrate consumption and also influencing the energy balance.	Ruetsch et al. 2005
Antipsychotic Drugs	The drug may increase appetite and body weight.	Aksoy 2016 Pronsky and Crowe 2012 Reekie et al. 2015 Kang et al. 2014 Emsley et al. 2015
Chlorpromazine	It may cause riboflavin and B_{12} deficiency.	Elmacioğlu 2007 Pronsky and Crowe 2012
Sleeping pills	The use of sleeping pills with alcohol and caffeine should be avoided.	FDA 2016 Ismail 2009
Zolpidem	It may interact with St John's wort.	Hojo et al. 2011
Triazolam	It may interact with grapefruit juice.	Hukkinen et al. 1995

MICROBIOTA AND DRUG METABOLISM

Currently, gastrointestinal microbiota is considered a potential therapeutic approach for drug discovery and therapy (Jia et al. 2008). It is well known that microbiota are involved in various chemical reactions such as acetylation, deacylation, decarboxylation, dehydroxylation, demethylation, and dehalogenation of drugs. Moreover, microbiota can shape drug metabolism of the host indirectly (Wilson and Nicholson 2017). In a comprehensive review, Sousa et al. (2008) provided an overview of the gastrointestinal microbiota, their drug substrates, and metabolic mechanisms. In the review, they concluded that microbiota should be considered in development process of drugs.

In recent years, gut microbiota and health interactions have been highlighted as an important emerging issue. Several studies have highlighted that different patterns of gut microbiota predict better health outcomes, and that gut microbiota interact with external sources that the host consumes, such as nutrients and drugs. Along with age, type of birth, physical activity, smoking and antibiotic use, diet pattern is one of the major factors that can modulate the gut microbiota (Laparra and Sanz 2010).

Results of recent studies reveal an interaction between diet, gut microbiome, and vagal gut-brain communication. These studies provide strong evidence for the role of food in physiology and pathology of the nervous system. High fat-induced diets lead to increased body fat accumulation and changes in gut microbiota (i.e. increased *Firmicutes/Bacteriodetes* ratio and Proteobacteria). High fat diets may also disrupt vagal gut-brain communication via microglia activation, as shown recently in Sprague-Dawley rats (Vaughn et al. 2017). Furthermore, low fat intake in conjunction with high fat and high sugar can alter the composition of the microbiota, increase circulating lipopolysaccharide levels, and may increase obesity risk via vagal remodeling (Sen et al. 2017). Given the strong influence of diet on the gut microbiota, diet may also alter drug pharmacokinetics.

CONCLUSION

Drugs used in the treatment of neurological and psychological diseases can interact with many foods and nutrients. As a result of these drug-food interaction, the expected outcomes may not be observed. In addition, drug toxicity may occur and the nutritional status may deteriorate via nutrient deficiencies. Furthermore, some food/nutrient-drug interactions may cause changes in body weight and energy balance via modulation of appetite. Genetic background is one of the main determinants of these interactions. In particular, neurological and psychological patients with specific gene polymorphisms can be at increased risk for food-drug interactions, compared to patients without the polymorphism. Moreover, microbiota can shape the drug metabolism of the host. Thus, microbiota alterations should also be considered while assessing diet/nutrient–drug interactions. When considering all interaction mechanisms and other related factors, prognosis of neurological and psychological diseases may deteriorate because of these secondary outcomes. Therefore, monitoring for food–drug interactions will be critical for determining the appropriate dosage and timing of drugs, and preventing adverse secondary outcomes. Knowledge of food-drug interactions is important for improving health of patients with neurological and psychological diseases, as well as for improving the effectiveness of treatments. To prevent food-drug interactions, there should be multidisciplinary collaboration between pharmacists, doctors, nurses and dieticians throughout the duration of the treatment protocol. Moreover, a nutrition program/diet prepared by a dietician will be helpful in monitoring and preventing nutritional deficiencies and body weight changes that occur from food-drug interactions. Taking these steps will help minimize adverse effects of food-drug interactions.

REFERENCES

Aggarwal A, Jethani S, Rohatgi R, Kalra J (2016) Selective serotonin re-uptake inhibitors (SSRIs) induced weight changes: a dose and duration dependent study on albino rats. J Clin Diagn Res 10: AF01.

Akbulut G (2009) Current Applications in Clinical Nutrition Therapy-IV: Nutritional Therapy in Neurological Disease (in Turkish). Nobel Tıp Kitapevleri, Ankara, Turkey.

Aksoy M (2016) Food and Drug Interaction (in Turkish). İstanbul Tıp Kitapevi, İstanbul, Turkey.

Antel J, Hebebrand J (2012) Weight-reducing side effects of the antiepileptic agents topiramate and zonisamide. Handb Exp Pharmacol 209: 433–466.

Armutcu F, Ozerol E, Gurel A, Kanter M, Vural H, Yakinci C, Akyol O (2004) Effect of long-term therapy with sodium valproate on nail and serum trace element status in epileptic children. Biol Trace Elem Res 102: 1–10.

Arslan M, Vurucu S, Balamtekin N, Unay B, Akin R, Kurt I, Ozcan O (2009) The effects of biotin supplementation on serum and liver tissue biotinidase enzyme activity and alopecia in rats which were administrated to valproic acid. Brain Dev 31: 405–410.

Bächle C, Lange K, Stahl-Pehe A, Castillo K, Holl RW, Giani G, Rosenbauer J (2015) Associations between HbA1c and depressive symptoms in young adults with early-onset type 1 diabetes. Psychoneuroendocrinology 55: 48–58.

Baek JH, Seo YH, Kim GH, Kim MK, Eun BL (2014) Vitamin D levels in children and adolescents with antiepileptic drug treatment. Yonsei Med J 55: 417–421.

Barreto Medeiros JM, Cabral Filho JE, De Souza SL, Freitas Silva SR, Mendes Da Silva C, Deiro TC, Monteiro JM, Guedes RCA, De Castro CMMB, Manhães De Castro R (2002) Early malnourished rats are not affected by anorexia induced by a selective serotonin reuptake inhibitor in adult life. Nutr Neurosci 5: 211–214.

Başoğlu S, Hasbay A, Gökmen H (1999) Food and Drug Interaction (in Turkish). Ankara: Beslenme Bilimleri ABD Yayını, Ankara, Turkey, p. 12–26.

Bender DA, Earl CJ, Lees AJ (1979) Niacin depletion in Parkinsonian patients treated with L-dopa, benserazide and carbidopa. Clin Sci 56: 89–93.

Ben-Menachem E (2007) Weight issues for people with epilepsy-a review. Epilepsia 48: 42–45.

Bochyńska A, Lipczyńska-Łojkowska W, Gugała-Iwaniuk M, Lechowicz W, Restel M, Graban A, Lipska B, Ryglewicz D (2012) The effect of vitamin B supplementation on homocysteine metabolism and clinical state of patients with chronic epilepsy treated with carbamazepine and valproic acid. Seizure 21: 276–81.

Bushra R, Aslam N, Khan AY (2011) Food-drug interactions. Oman Med J 26: 77.

Bykov I, Mal'tsev A, Gurinovich V, Nefedov L (2004) Biochemical basis of valproic acid toxicity: role of oxidative stress and effects of L-carnitine. Biomed Khim 50: 384–389.

Castro-Gago M, Pérez-Gay L, Gómez-Lado C, Castiñeiras-Ramos DE, Otero-Martínez S, Rodríguez-Segade S (2011) The influence of valproic acid and carbamazepine treatment on serum biotin and zinc levels and on biotinidase activity. J Child Neurol 26: 1522–1524.

Chandrasekaran S, Patil S, Suthar R, Attri SV, Sahu JK, Sankhyan N, Tageja M, Singhi P (2017) Hyperhomocysteinaemia in children receiving phenytoin and carbamazepine monotherapy: a cross-sectional observational study. Arch Dis Child 102: 346–351.

Choi JH, Ko CM (2017) Food and drug interactions. J Lifestyle Med 7: 1–9.

Cucca A, Mazzucco S, Bursomanno A, Antonutti L, Di Girolamo F, Pizzolato G, Koscica N, Gigli GL, Catalan M, Biolo G (2015) Amino acid supplementation in l-dopa treated Parkinson's disease patients. Clin Nutr 34: 1189–1194.

Davison AS, Milan AM, Roberts NB (2011) The consequences of valproate overdose. Clin Chem 57: 1233–1237.

Deeg MA, Lipkin EW (1996). Hypoglycemia associated with the use of fluoxetine. West J Med 164: 262–263.

Di Rosa G, Lenzo P, Parisi E, Neri M, Guerrera S, Nicotera A, Alibrandi A, Germanò E, Caccamo D, Spanò M, Tortorella G (2013) Role of plasma homocysteine levels and MTHFR polymorphisms on IQ scores in children and young adults with epilepsy treated with antiepileptic drugs. Epilepsy Behav 29: 548–551.

Dysken MW, Cumming RJ, Channon RA, Davis JM (1979) Drug interaction between ascorbic acid and fluphenazine. JAMA 241: 2008.

Elmacıoğlu F (2007) Food and drug interaction (in Turkish). Turkiye Klinikleri Journal of Internal Medical Sciences 3: 108–120.

Emsley R, Asmal L, Chiliza B, du Plessis S, Carr J, Kidd M, Malhotra AK, Vink M, Kahn RS (2015) Changes in brain regions associated with food-intake regulation, body mass and metabolic profiles during acute antipsychotic treatment in first-episode schizophrenia. Psychiatry Res 233: 186–193.

Eriksson T, Walinder J (1998) Amitriptyline and clomipramine increase the concentration of administered L-tryptophan in the rat brain. J Pharm Pharmacol 50: 1133–1137.

Fekkes D, Timmerman L, Pepplinkhuizen L (1997) Effects of clomipramine on plasma amino acids and serotonergic parameters in panic disorder and depression. Eur Neuropsychopharmacol 7: 235–239.

Fernandez N, Garcia JJ, Diez MJ, Sahagun AM, Díez R, Sierra M (2010) Effects of dietary factors on levodopa pharmacokinetics. Expert Opin Drug Metab Toxicol 6: 633–642.

Flockhart DA (2012) Dietary restrictions and drug interactions with monoamine oxidase inhibitors: an update. J Clin Psychiatry 73: 17–24.

Fong CY, Kong AN, Poh BK, Mohamed AR, Khoo TB, Ng RL, et al (2016) Vitamin D deficiency and its risk factors in Malaysian children with epilepsy. Epilepsia 57: 1271–1279.

Food and Drug Administration (FDA) (2016) Avoid food-drug interactions. http//www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/GeneralUseofMedicine/UCM229033.pdf.

Fukuda M, Kawabe M, Takehara M, Iwano S, Kuwabara K, Kikuchi C, Wakamoto H, Morimoto T, Suzuki Y, Ishii E (2015) Carnitine deficiency: Risk factors and incidence in children with epilepsy. Brain Dev 37: 790–796.

Gorgone G, Curro M, Ferlazzo N, Parisi G, Parnetti L, Belcastro V, Tambasco N, Rossi A, Pisani F, Calabresi P, Ientile R, Caccamo D (2012) Coenzyme Q10, hyperhomocysteinemia and MTHFR C677T polymorphism in levodopa-treated Parkinson's disease patients. Neuromolecular Med 14: 84–90.

Gorjipour F, Asadi Y, Osguei NK, Effatkhah M, Samadikuchaksaraei A (2013) Serum level of homocysteine, folate and vitamin-B12 in epileptic patients under carbamazepine and sodium valproate treatment: a systematic review and meta-analysis. Iran Red Crescent Med J 15: 249.

Greenblatt DJ, Harmatz JS, Singh NN, Roth T, Harris SC, Kapil RP (2013) Influence of food on pharmacokinetics of zolpidem from fast dissolving sublingual zolpidem tartrate tablets. J Clin Pharmacol 53: 1194–1198.

Günaydın ZY, Özer FF, Karagöz A, Bektaş O, Karataş MB, Vural A, Bayramoğlu A, Çelik A, Yaman M (2016) Evaluation of cardiovascular risk in patients with Parkinson disease under levodopa treatment. J Geriatr Cardiol 13: 75.

Hojo Y, Echizenya M, Ohkubo T, Shimizu T (2011) Drug interaction between St John's wort and zolpidem in healthy subjects. J Clin Pharm Ther 36: 711–715.

Hosseinpour F, Ellfolk M, Norlin M, Wikvall K (2007) Phenobarbital suppresses vitamin D 3 25-hydroxylase expression: a potential new mechanism for drug-induced osteomalacia. Biochem Biophys Res Commun 357: 603–607.

Hukkinen SK, Varhe A, Olkkola KT, Neuvonen PJ (1995) Plasma concentrations of triazolam are increased by concomitant ingestion of grapefruit juice. Clin Pharmacol Ther 58: 127–131.

Ismail MYM (2009) Drug-food interactions and role of pharmacist. Asian J Pharm Clin Res 2: 1–10.

Jia W, Li H, Zhao L, Nicholson JK (2008) Gut microbiota: a potential new territory for drug targeting. Nat Rev Drug Discov 7: 123–129.

Jiang HY, Chen HZ, Hu XJ, Yu ZH, Yang W, Deng M, et al. (2015) Use of selective serotonin reuptake inhibitors and risk of upper gastrointestinal bleeding: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 13: 42–50.

Kang SH, Lee JI, Han HR, Soh M, Hong JP (2004) Polymorphisms of the leptin and HTR2C genes and clozapine-induced weight change and baseline BMI in patients with chronic schizophrenia. Psychiatr Genet 24: 249–256.

Karabiber H, Sonmezgoz E, Ozerol E, Yakinci C, Otlu B, Yologlu S (2003) Effects of valproate and carbamazepine on serum levels of homocysteine, vitamin B12, and folic acid. Brain Dev 25: 113–115.

Katayama H, Mizukami K, Yasuda M, Hatae T (2016) Effects of carnitine on valproic acid pharmacokinetics in rats. J Pharm Sci 105: 3199–3204.

Kirmani BF, Robinson DM, Fonkem E, Graf K, Huang JH (2016) Role of anticonvulsants in the management of posttraumatic epilepsy. Front Neurol 7: 32.

Laparra JM, Sanz Y (2010) Interactions of gut microbiota with functional food components and nutraceuticals. Pharmacol Res 61: 2019–2025.

Lee SH, Yu J (2015) Risk factors of vitamin D deficiency in children with epilepsy taking anticonvulsants at initial and during follow-up. Ann Pediatr Endocrinol Metab 20: 198–205.

Magni LR, Ferrari C, Rossi G, Staffieri E, Uberti A, Lamonaca D, Boggian I, Merlin S, Primerano G, Mombrini A, Poli R, Saviotti FM, Caldera MT, Zanotti L, Rossi R (2017) Superwellness Program: a cognitive-behavioral therapy-based group intervention to reduce weight gain in patients treated with antipsychotic drugs. Rev Bras Psiquiatr 39: 244–251.

Malcolm D, Yu P, Bowen R, O'Donovan C, Hawkes J, Hussein M (1994) Phenelzine reduces plasma vitamin B6. J Psychiatry Neurosci 19: 332–334.
Marahatta A, Bhandary B, Jeong SK, Kim HR, Chae HJ (2014) Soybean greatly reduces valproic acid plasma concentrations: A food–drug interaction study. Sci Rep 4: 4362.
Martin C, Han H, Anton S, Greenway F, Smith S (2009) Effect of valproic acid on body weight, food intake, physical activity and hormones: results of a randomized controlled trial. J Psychopharmacol 23: 814–825.
McIntyre RS, Soczynska JK, Konarski JZ, Kennedy SH (2006). The effect of antidepressants on glucose homeostasis and insulin sensitivity: synthesis and mechanisms. Expert Opin Drug Saf 5: 157–168.
Miyaoka T, Yasukawa R, Tsubouchi K, Miura S, Shimizu Y, Sukegawa T, et al. (2003) Successful treatment of nocturnal eating/drinking syndrome with selective serotonin reuptake inhibitors Int Clin Psychopharmacol 18: 175–177.
Mock DM, Mock NI, Nelson RP, Lombard KA (1998) Disturbances in biotin metabolism in children undergoing long-term anticonvulsant therapy. J Pediatr Gastroenterol Nutr 26: 245–250.
Moreno FA, Macey H, Schreiber B (2005) Carnitine levels in valproic acid-treated psychiatric patients: a cross-sectional study. J Clin Psychiatry 66: 555–558.
Munisamy M, Al-Gahtany M, Tripathi M, Subbiahc V (2015) Impact of MTHFR (C677T) gene polymorphism on antiepileptic drug monotherapy in North Indian epileptic population. Ann Saudi Med 35: 51.
Nakamura M, Nagamine T (2015) The effect of carnitine supplementation on hyperammonemia and carnitine deficiency treated with valproic acid in a psychiatric setting. Innov Clin Neurosci 12: 18.
Ni G, Qin J, Fang Z, Chen Y, Chen Z, Zhou J, Zhou L (2014) Increased homocysteine levels in valproate-treated patients with epilepsy: a meta-analysis. BMJ Open 4: e004936.
Ogo Y, Sunagane N, Ohta T, Uruno T (2005) Banana juice reduces bioavailability of levodopa preparation. J Pharm Soc Jap 125: 1009–1011.
Oliveira I, Silva L, Borges M, Cruz O, Tessmann J, Motta J, et al (2017) Interactions between lifestyle and MTHFR polymorphisms on homocysteine concentrations in young adults belonging to the 1982 Pelotas Birth Cohort. Eur J Clin Nutr 71: 259–266.
Ornoy A, Weinstein-Fudim L, Ergaz Z (2017) Antidepressants, antipsychotics,and mood stabilizers in pregnancy: what do we know and how should we treat pregnant women with depression. Birth Defects Res 109: 933–956.
Otles S, Senturk A (2014) Food and drug interactions: a general review. Acta Sci Pol Technol Aliment 13: 89–102.
Pronsky Z, Crowe J (2012) Krause's Food and Nutrition Care Process. Mahan L, Escott-Stump S, Raymond J, editors. USA: Elsevier; 209–228 p.
Qureshi GA, Qureshi AA, Devrajani BR, Chippa M, Syed SA (2008) Is the deficiency of vitamin B12 related to oxidative stress and neurotoxicity in Parkinson's patients? CNS Neurol Disord Drug Targets 7: 20–27.
Rathman SC, Gregory JF, McMahon RJ (2003) Pharmacological biotin supplementation maintains biotin status and function in rats administered dietary carbamazepine. J Nutr 133: 2857–2862.
Reekie J, Hosking S, Prakash C, Kao KT, Juonala M, Sabin M (2015) The effect of antidepressants and antipsychotics on weight gain in children and adolescents. Obes Rev 16: 566–580.
Rezaei S, Shab-Bidar S, Abdurahman AA, Djafarian K (2017) Oxcarbazepine administration and the serum levels of homocysteine, vitamin B12 and folate in epileptic patients: A systematic review and meta-analysis. Seizure 45: 87–94.
Rozycka A, P Jagodzinski P, Kozubski W, Lianeri M, Dorszewska J (2013) Homocysteine level and mechanisms of injury in Parkinson's disease as related to MTHFR, MTR, and MTHFD1 genes polymorphisms and LDopa treatment. Curr Genomics 14: 534–542.
Ruetsch O, Viala A, Bardou H, Martin P, Vacheron M (2005) Psychotropic drugs induced weight gain: a review of the literature concerning epidemiological data, mechanisms and management. Encephale 31: 507–16.
Sarangi SC, Tripathi M, Kakkar AK, Gupta YK (2014) Effect of antiepileptic therapy on trace elements status in Indian population in a tertiary care hospital from northern India: A cross sectional study. Epilepsy Res108: 917–927.
Sathiya Priya C, Bhavani K, Anuradha CV (2016) High-calorie diet inflates steatogenic effects of valproic acid in mice. Toxicol Mech Methods 26: 112–121.
Schlegel-Zawadzka M, Nowak G (2000) Alterations in serum and brain trace element levels after antidepressant treatment. Part II. Copper. Biol Trace Elem Res 73: 37–45.
Seligmann H, Potasman I, Weller B, Schwartz M, Prokocimer M (1998) Phenytoin-folic acid interaction: a lesson to be learned. Clin Neuropharmacol 22: 268–272.
Semmler A, Moskau-Hartmann S, Stoffel-Wagner B, Elger C, Linnebank M (2013) Homocysteine plasma levels in patients treated with antiepileptic drugs depend on folate and vitamin B12 serum levels, but not on genetic variants of homocysteine metabolism. Clin Chem Lab Med 51: 665–669.
Sen T, Cawthon CR, Ihde BT, Hajnal A, DiLorenzo PM, de La Serre CB, Czaja K (2017) Diet-driven microbiota dysbiosis is associated with vagal remodeling and obesity. Physiol Behav 173: 305–317.
Sener U, Zorlu Y, Karaguzel O, Ozdamar O, Coker I, Topbas M (2006) Effects of common anti-epileptic drug monotherapy on serum levels of homocysteine, vitamin B12, folic acid and vitamin B6. Seizure 15: 79–85.
Sousa T, Paterson R, Moore V, Carlsson A, Abrahamsson B, Basit AW (2008) The gastrointestinal microbiota as a site for the biotransformation of drugs. Int J Pharm 363: 1–25.
Vaughn AC, Cooper EM, DiLorenzo PM, O'Loughlin LJ, Konkel ME, Peters JH, Hajnal A, Sen T, Lee SH, de La Serre CB, Czaja K (2017) Energy-dense diet triggers changes in gut microbiota, reorganization of gut-brain vagal communication and increases body fat accumulation. Acta Neurobiol Exp 77: 18–30.
Vernon GM (2013) Sex, drugs and alcohol: drug interactions of concern to consumers. Aust Prescr 36: 46–82.
Vestergaard P (2015) Effects of antiepileptic drugs on bone health and growth potential in children with epilepsy. Pediatr Drugs 17: 141–150.
Volz HP, Gleiter CH (1998) Monoamine oxidase inhibitors. A perspective on their use in the elderly. Drugs Aging 13: 341–355.
Wei F, Crain AL, Whitebird RR, Godlevsky OV, O'Connor PJ (2009) Effects of paroxetine and sertraline on low-density lipoprotein cholesterol. CNS Drugs 23: 857–865.
Wilson ID, Nicholson JK (2017) Gut microbiome interactions with drug metabolism, efficacy, and toxicity. Transl Res 179: 2014–2022.
World Health Organization (WHO) (2006) Neurological disorders public health challenges. http//www.who.int/mental_health/neurology/neurological_disorders_report_web.pdf.
Wu M, Huang C, Liou Y, Wang C, Lee S (2008) Glucose-insulin homeostasis, lipid profiles and GH-IGF-IGFBP axis in clozapine-treated schizophrenic obesity versus non-psychiatric obesity. Int J Obes 32: 436.
Wu SP, Shyu MK, Liou HH, Gau CS, Lin CJ (2004) Interaction between anticonvulsants and human placental carnitine transporter. Epilepsia 45: 204–210.
Xie Y, Feng H, Peng S, Xiao J, Zhang J (2017) Association of plasma homocysteine, vitamin B12 and folate levels with cognitive function in Parkinson's disease: A meta-analysis. Neurosci Lett 636: 190–195.
Yilmaz Y, Tasdemir HA, Paksu MS (2009) The influence of valproic acid treatment on hair and serum zinc levels and serum biotinidase activity. Eur J Paediatr Neurol 13: 439–443.
Yohn CN, Gergues MM, Samuels BA (2017) The role of 5-HT receptors in depression. Mol Brain 10: 28.
Yuan Y, Tsoi K, Hunt RH (2006) Selective serotonin reuptake inhibitors and risk of upper GI bleeding: confusion or confounding? Am J Med 119: 719–727.
Zhang LF, Liu LS, Chu XM, Xie H, Cao LJ, Guo C (2014) Combined effects of a high-fat diet and chronic valproic acid treatment on hepatic steatosis and hepatotoxicity in rats. Acta Pharmacol Sin 35: 363.