





# Healthy Eating, Physical Activity, and Sleep Hygiene (HEPAS) as the Winning Triad for Sustaining Physical and Mental Health in Patients at Risk for or with Neuropsychiatric Disorders: Considerations for Clinical Practice

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**Abstract:** Neuropsychiatric disorders stem from gene-environment interaction and their development can be, at least in some cases, prevented by the adoption of healthy and protective lifestyles. Once full blown, neuropsychiatric disorders are prevalent conditions that patients live with a great burden of disability. Indeed, the determinants that increase the affliction of neuropsychiatric disorders are various, with unhealthy lifestyles providing a significant contribution in the interplay between genetic, epigenetic, and environmental factors that ultimately represent the pathophysiological basis of these impairing conditions. On one hand, the adoption of Healthy Eating education, Physical Activity programs, and Sleep hygiene promotion (HEPAS) has the potential to become one of the most suitable interventions to reduce the risk to develop neuropsychiatric disorders, while, on the other hand, its integration with pharmacological and psychological therapies seems to be essential in the overall management of neuropsychiatric disorders in order to reduce the disability and improve the quality of life of affected patients. We present an overview of the current evidence in relation to HEPAS components in the prevention and management of neuropsychiatric disorders and provide suggestions for clinical practice.

**Keywords:** neuropsychiatry, diet, motor activity, sleep, quality of health care

## Introduction

Neurological and psychiatric disorders are among the non-communicable diseases that are associated the most with several years lived with disability, and are currently, and will likely become progressively, part of a pervasive illness affecting physical and mental fitness.<sup>1</sup> Indeed, these conditions continue to show a large prevalence in the general population and, in the last 10 years, a further increase in all-age years lived with disabilities has been observed for both neurological (mean increase in counts of 17.8%) and mental (mean increase in counts of 13.5%) disorders.<sup>2</sup> These conditions encompass a wide range of illnesses that affect brain anatomy and function, such as schizophrenia spectrum disorders, mood and anxiety disorders, cognitive disorders with collateral alterations of attention, mood, emotion, and memory. Diagnosis and management is often arduous because symptoms may derive from neurological, psychological, or iatrogenic causes and can easily lead to poor course and outcome. The overlap of

etiopathogenetic phenomena led to the existence of multifaceted spectra and multiple specifiers, such as the “with anxious distress” in major depressive episodes, the schizo-obsessive<sup>3</sup> phenotype, or the tic-related obsessive-compulsive disorder,<sup>4</sup> thus stressing the need for a holistic approach in neuropsychiatric disorders now more than ever. Although the current psychotropic drug- and psychotherapy-centered approaches are deemed effective for many patients, some show pharmacological refractoriness or are unable to tolerate side effects, and physical treatments have been largely implemented.<sup>5</sup> Despite the fact that determinants increasing the burden of neuropsychiatric diseases are various, the behavioral factors still provide the highest contribution over metabolic and environmental/occupational risks. According to the Institute for Health Metrics and Evaluation (IHME) classification, the behavioral risks mainly comprise bad dietary habits, smoking, malnutrition, alcohol use, and low physical activity.<sup>2</sup> A consistent body of literature identifies eating patterns and physical activity as crucial determinants for physical and mental fitness, the latter being associated to a good sleep. In fact, the brain governs basic sleep/wake cycle, behavioral states and shapes cognitive functions, and sleep disturbances are often associated to a stressed body and mind. Sleep changes are often the earliest signs of several neuropsychiatric disorders, but have also been considered as state markers for mental illnesses, partly as our genetic makeup.<sup>6</sup>

For the purpose of the present overview, data from Google Scholar, PubMed, and Scopus databases were searched and reviewed, focusing on publications regarding diet, physical fitness, and sleeping patterns in the prevention and overall management of neuropsychiatric disorders, mainly encompassing schizophrenia spectrum disorders, mood disorders, anxiety disorders, and neurocognitive disorders. The search considered relevant studies to introduce the rationale for each section and discuss retrospective and prospective clinical trials, systematic and non-systematic reviews, meta-analyses, guidelines and expert opinions. Our ultimate aim was to deliver practical suggestions for neuropsychiatrists and clinical psychologists that can support the application of a program covering Healthy Eating education, Physical Activity planning, and Sleep hygiene (HEPAS).

## Healthy Eating in Neuropsychiatry

Eating is essential to life, as well as breathing, sleeping, and evacuating. We eat for hunger, for pleasure, for boredom, and for addiction.<sup>7</sup> Most people eat three meals plus snacks daily,

which is an unusual eating pattern from an evolutionary perspective,<sup>8</sup> as we have been purely hunters and gatherers for thousands of years. Food had always influenced our mental abilities: the ability to harness fire and cook food allowed the brain of the *Homo erectus* to grow over 1.8 million years ago,<sup>9</sup> with the progressive hypotrophy of masseter and pterygoid muscles allowing cranial development since the consumption of raw and fibrous meat was abandoned. Brain activity is constant, with activity peaks that depend on what the mind is involved in. This activity requires relentless supply of fuel that is mainly glucose, but may also be of non-carbohydrate origin, with a variety of crucial vitamins, minerals, and trace elements integrating core processes. Mechanisms through which diet influences brain functions are likely to be numerous and composite. They mainly comprise the modulation of neuronal energy metabolism and the epigenetic regulation of synaptic plasticity.<sup>10</sup> As such, foods can affect brain function according to the content or lack of nutrients.<sup>11,12</sup> Food components have a role in brain development since the early orchestration of morphogenic signaling<sup>13</sup> towards late fetal and early post-natal life,<sup>14</sup> till the modulation of adult neurogenesis. Foods routinely affect brain even if not consumed with the involvement of rewarding mechanisms.<sup>15</sup> Substantial improvements have been achieved in the field of nutraceuticals, with antioxidant properties, immune system modulation, and neurotrophic activity<sup>16</sup> being just some of the effects attributed to food substances that are concentrated and sold as dietary supplements.<sup>16–18</sup> However, while nutrients are thoughtfully absorbed by the body, non-nutritive compounds less easily cross physiological barriers and targeted drug delivery system would be needed to properly enhance their bioavailability.<sup>19</sup>

Hunters and gatherers no longer exist, but food availability is almost excessively guaranteed with a wealth of ready-to-eat, high-calorie, tasty products, as if there was the threat of food famine. Most people have forgotten that food is medicine.<sup>20</sup> In the following paragraphs, we describe and discuss: I) the reciprocal relationship between diet and neuropsychiatric disorders, II) existing methods to assess eating habits, III) practical suggestions to promote healthy eating.

## The Reciprocal Relationship Between Diet and Neuropsychiatric Disorders

The existence during early stages of life span of a bidirectional relationship between healthy diet and superior mental health has been shown by many epidemiologic

studies.<sup>21</sup> Single food components are considered as significant exposure variables that concur to cause various neuropsychiatric conditions. For instance, even if neurons primarily rely on glucose to function, a high intake of sugars may be noxious and may increase the risk for depression<sup>22</sup> and neurocognitive impairment.<sup>23,24</sup> Indeed, the importance of the dietary pattern as a modifiable risk factor for mental illness gave birth to the nutritional psychiatry field.<sup>25,26</sup> Unfortunately, poor dietary choices are made by patients suffering from schizophrenia,<sup>27</sup> tics, obsessions, and compulsions,<sup>28–31</sup> thus further exposing patients to nutritional deficiencies that are associated with worse mental health issues.<sup>32</sup> Moreover, unhealthy diet was reported for bipolar patients<sup>33</sup> and patients with depressive and anxiety disorders.<sup>34</sup> Drug therapy can easily predispose to worse physical health, being some psychotropics obesogenic in nature.<sup>35</sup> As soon as an individual adopts an unhealthy dietary pattern, his mental functions could be exposed to negative anatomical variations in critical brain areas, such as the hippocampus.<sup>36,37</sup> Vascular impairments, because of glycaemic alterations, may have a role in the development of dementia<sup>38</sup> and psychiatric conditions.<sup>22</sup> Cognitive deficits were found in individuals consuming sugar-sweetened beverages.<sup>39</sup> A new frontier in nutritional psychiatry is stemming from research targeting the modulation of the gut microbiota. In fact, diet is a direct modulator of gut microbiota, whose role has been extensively studied not only in association with neuropsychiatric diseases, but also with subclinical emotional states,<sup>40</sup> possibly evoked by the production of specific neurotransmitters.<sup>12</sup> Besides having a role in food and drug metabolism, gut microbiota composition seems to either influence or be influenced by numerous neuropsychiatric conditions, through the induction of dysbiosis and alteration of gut permeability, which can, in turn, release pro-inflammatory mediators, activate the immune system and induce a state of low-grade inflammation.<sup>41</sup> All these mechanisms can alter brain functioning at various levels, with repercussions on mental health.

## Existing Methods to Assess Eating Habits

Diet quality, quantity, meal timing, and environment are four features characterizing eating patterns. Past dietetic habits may be meticulously analyzed through dietetic history questionnaires (eg, those developed by the National Cancer Institute can be found here <https://epi.grants.cancer.gov/dhq3/>), whereas more recent eating behaviors can be derived from a seven-day food diary that can be either

paper-based or web-based.<sup>42</sup> Dietetic history questionnaires are certainly more time-consuming, consisting of 135 food and beverage items and 26 dietary supplement questions. Objective evaluations of eating behaviors are quite difficult to acquire, and subjective questionnaires are widely used. Seven-day food diary is the most suitable method for an objective analysis, but also body weight changes may indeed objectively reflect all the four features of eating patterns. Dietary habits of neuropsychiatric patients might be investigated through less time-consuming tests that evaluate how similar patient's diet is to the Mediterranean dietary pattern, which is the one recognized as the healthiest. In fact, this diet has been implemented worldwide from European to American populations.<sup>43</sup> It is mainly characterized by appropriate intakes of vegetables, fruits, whole grains, dairy products, seafood, lean meats and poultry, eggs, legumes, nuts, olive oil, and alcohol. Calories from added sugars and saturated fats should be limited and sodium intake should be reduced. Healthy eating is inexpensive, and low-income individuals can afford it.<sup>44</sup> Higher adherence to these dietary guidelines is associated with reduced total, cardiovascular, and cancer mortality risks<sup>45</sup> and better general physical health.<sup>46</sup> Average intakes of different food groups are far from recommended amounts: about 75% of the Americans has an eating pattern that is low in vegetables, fruits, dairy, and oils, and most of subjects exceed the recommendations for added sugars, saturated fats, and sodium,<sup>47</sup> with important differences during the transition from adolescence to young adulthood.<sup>48</sup> In younger patients, the test of Serra-Majem and colleagues can be used for non-quantitatively evaluate the adherence to the Mediterranean diet.<sup>49</sup> The score, which was validated in healthy Spanish children and youths, consists of 16 questions with either positive (+1) or negative (–1) connotation, with the sum identifying the Mediterranean quality among three levels (ie, low, improvements needed, optimal). For adults, the literature-based adherence score to the Mediterranean diet of Sofi and colleagues might be particularly convenient.<sup>50</sup> The score, who was estimated from data coming from over 4 million subjects, ranges from 0 (lowest Mediterranean diet adherence) to 18 points (highest Mediterranean diet adherence), and comprises 9 quantity-based questions to be answered with the assignment of 0, 1, or 2 points each according to the higher Mediterranean connotation. Both suggested indexes can be easily used in clinical practice and they take about 5 mins each to be completed.

## Practical Suggestions to Promote Healthy Eating

An adjunctive-personalized dietary advice and a nutritional counselling support, focusing on healthy eating recommendations, were found to be effective in reducing symptoms in patients with unipolar depression.<sup>51</sup> Even small changes may be sufficient to achieve greater advantages: the addition of a specific food category, such as nuts,<sup>52</sup> to an individual's eating habit may be effective in the integrated treatment of depression. Moreover, the supplementation with omega-3 fatty acids, zinc, B vitamins have been often studied in neuropsychiatric populations, with debated results.<sup>53,54</sup> Targeted probiotic supplementations could be also considered an encouraging integrative approach.<sup>55</sup> In clinical practice, patients should be first educated to pursue an optimal quality of the diet. In some psychiatric patients, it is important to avoid restrictive and/or selective eating patterns.<sup>29</sup> Because people have different preferences for specific foods, it is important to understand whether quantity, quality, or timing is the most beneficial intervention for them. Patients should be informed that quality and timing are surely more important than quantity, at least for weight management.<sup>56</sup> A nutritional counseling may be more pragmatic as part of dietetic sessions to be taken with the support of written information, meal ideas, recipe examples, shopping lists, label reading instructions, and food security information.<sup>30,57</sup> The tailored dietetic plan should eventually be designed to be easy to follow, sustainable, palatable, and satiating,<sup>51</sup> with the eventual meal assistance support to convey motivational eating. The general aim should be to instruct patients to follow a balanced diet that contains suitable options for carbohydrates, proteins, lipids, vegetables, and fruits. Impulsive eating may be circumvented through the consumption of snacks in-between meals. Early identification of low baseline adherence to a specific diet, learned helplessness (ie, perceived absence of control to achieve any success) for previous attempts to lose body weight, fear or gain in body weight because of pharmacological therapy, or displeasure of body image should be investigated.<sup>29</sup> Moreover, family environment affecting food habits should be always explored, especially for younger patients.<sup>28</sup> Pathological behaviors might vitiate food habits, therefore a thoughtful assessment should be always considered.<sup>29</sup> Neuropsychiatric patients may use dietary supplements without informing their doctor, as they may consider the use of supplements not worth of note or feel uncomfortable in admitting their choice of

complementary remedies. Patients can present misperceptions about the efficacy of certain supplements, and a more scientific education should be provided for these cases.<sup>12</sup> Dietetic sessions should include information about conditional recommendations to avoid foods or beverages known to interfere with drug pharmacokinetic/pharmacodynamic profile.<sup>29,58</sup>

## Physical Activity in Neuropsychiatry

As hunters and gatherers, our ancestors trekked miles every day and had the highest activity levels<sup>59</sup> compared both to the present day and to our past apelike existence. In fact, our ancestors initially transitioned from a sedentary simian lifestyle to a more physically demanding hunter-gatherer one, when they started carrying out foraging tasks. This evolutionary process is believed to have promoted brain development because of the combination of aerobic activity with control of motor systems, spatial navigation, memory, executive functions including decision making and planning, and control of sensory and attentional systems.<sup>60</sup> "Until recently, all of us were athletes".<sup>61</sup> It is worth of note that not only the lowest level of physical activity, but also the extensively and uninterrupted sedentary behavior are risk factors for non-communicable diseases. Keeping active improves cardiopulmonary and musculoskeletal systems, which in turn ameliorate the mechanical potential of the body. The more the physical activity, the more the branching of blood capillaries and pruning of neuronal cells.<sup>62,63</sup> Physical activity affects levels of neurotransmitters, endorphins, and neurotrophic factors, such as the brain-derived neurotrophic factor, which are implicated in body and mental functioning.<sup>64</sup> An active lifestyle increases the antioxidant capacity and boosts the immune system (eg, myokines), thus rendering the body less vulnerable to both disease and cognitive decline. Common cellular pathways important for neurogenesis and plasticity may be synergistically promoted by physical exercise and food components.<sup>65</sup>

Nowadays, we are provided with excessive labor-saving innovations, such as cars, elevators, and escalators, which prevent us from significantly increasing our heart rate or breaking a sweat for days. "Few jobs require physical activity and most of us have little inclination to exercise in our spare time ... Let's help each other exercise more. In fact, it's what we evolved to do".<sup>61</sup> Exercise is medicine.<sup>66</sup> In the following paragraphs, we discuss and describe: I) the reciprocal relationship between physical fitness and neuropsychiatric disorders, II) existing methods

to assess physical activity levels, III) practical suggestions to promote physical activity.

## The Reciprocal Relationship Between Physical Fitness and Neuropsychiatric Disorders

The less a subject moves, the more he appears to be exposed to a higher risk of anxiety and depressive disorders,<sup>67,68</sup> cognitive decline and dementia.<sup>69</sup> Other than low physical activity, also sedentary behaviors should be reasonably avoided. Of note, different types of sedentary behaviors, such as television viewing and reading, may have a different impact on cognitive development,<sup>70</sup> thus suggesting that a hierarchy exists among sedentary activities, with some having to be preferred over others. In terms of physical commitment, reading and watching television are comparable activities, but most likely require different degrees of cognitive and emotional commitment as was showed by previous results comparing television viewing and regular computer use.<sup>71</sup> Indeed, screen sedentary behavior are associated, among other routinely behaviors, with greater distress.<sup>72</sup> Normally, maintaining an active outdoor lifestyle promotes mental health and mentally active subjects are those who exercise the most,<sup>73</sup> but this is not always true: professional athletes may suffer from brain disorders, with important performance affections, and these conditions gave birth, similarly to the nutritional psychiatry field, to sport psychiatry.<sup>74</sup> To this extent, the positive effects of an increased physical activity on mental distress cannot be always explained by physiological factors associated with ameliorated hormonal responses or endorphin production. The bi-directional relationship between a healthy brain and physical fitness is not a new concept<sup>75,76</sup> and many cross-sectional studies showed that people suffering from severe mental illness, such as schizophrenia, bipolar disorder, and major depressive disorder, have very low levels of physical activity in relation with longer illness duration and drug use.<sup>77</sup> Not only the lowest physical activity levels, but even much time spent being sedentary are behavioral features of those subjects with severe neuropsychiatric disorders.<sup>78,79</sup> Individuals who exercise the most may have a larger total brain volume, with the incremental physical activity having different effects on multiple brain regions.<sup>80</sup> As previously mentioned, the amelioration of hemodynamic responses may be at the basis of brain modifications upon physical exercise, extraordinarily mirroring cardiovascular

improvements and the acquisition of a general physical and psychological health.

## Existing Methods to Assess Physical Activity Levels

What does “move enough” mean? Quality, quantity, timing, and environment are important specifiers of physical activity programs. The quality of physical activity comprises the intensity (ie, effort level) and type, which vary between people according to demographic and health status. Endurance, muscle-strengthening, stretching, and balance activities are the main type categories, and they are all dependent on the environment (eg, outdoor, indoor, at school, watersports, mountain sports). Quantity comprises the duration (length of training) and frequency (times per week), while the timing means the moment of the day. Objective assessment of the usual body activity, in terms of energy consumed, may derive from actigraphy, which is a non-invasive method for monitoring rest/activity cycles.<sup>81</sup> To record physical activity, actigraphy devices (eg, single or multiple axis accelerometers) are usually worn on the wrist to record movements that can be used to estimate wavering parameters with the support of computerized algorithms. Subjective questionnaires may also be useful in order to obtain a different perceptive information, but they show more variability in properties of methodological effectiveness than objective measures,<sup>82</sup> such as accelerometer/activity monitor, as the latter allows examining the motion in free-living environments.<sup>83</sup> Reliable questionnaires are available for physical activity surveillance at the population level to collect data at work, for travelling to and from places, and for recreational activities (<https://www.who.int/ncds/surveillance/steps/GPAQ/en/>), but they seem to be outdated by last generation smartphones with built-in accelerometry.<sup>84</sup> Diverse physical activity guidelines are available online (<https://health.gov/paguidelines/second-edition/>) with infographics that can be more suitable for the public population. To achieve at least 150 mins of moderate to vigorous physical activity a week plus muscle-strengthening activities at least 2 days a week is recommended by the physical activity guidelines for Americans,<sup>85</sup> with similar advices from those of the World Health Organization and specific key objectives are available for preschool-aged children, adolescents, adults and older adults. However, more than 80% of adolescents is not active enough, together with 1 in 4 adults,<sup>86</sup> and the overall picture could be worse for

people suffering from mental illnesses. In clinical practice, all different neuropsychiatric patient groups can be daily monitored with wrist-mounted motion sensors, which are very useful for measuring total energy expenditure,<sup>87</sup> thus observing the adherence to exercise programs. An actigraphy device worn on the non-dominant wrist for 2 weeks is able to give not only motor activity, but also sleep duration data in patients, with associations being reported between motor activity and mood.<sup>88</sup> Collected data from daily monitoring are then downloaded to a computer for display and analysis of activity/inactivity that, in turn, can be further analyzed to estimate the rest-activity circadian rhythms.<sup>89</sup>

## Practical Suggestions to Promote Physical Activity

Rather different physical exercise interventions had all positive clinical effects in patients with schizophrenia, unipolar depression, Alzheimer's disease, Huntington's disease, Parkinson's disease, and multiple sclerosis.<sup>90</sup> Many professionals state that the prescription of physical activity interventions should be placed on a par with drug prescription, but this implies that neuropsychiatrists "know how to prescribe, monitor, and evaluate the effectiveness of the exercise prescribed".<sup>91</sup> However, this is not often the case and this obstacle must be overcome by the multi-disciplinary approach with the support of the exercise trainer. It is important to note that while dietary guidelines are very precise in terms of "what to eat" and "how much", physical activity guidelines are still much generalized. Various efforts and sport type combinations may have different mental health outcomes. While there are only limited ways of healthy eating (ie, the Mediterranean pattern), for physical activity it can be assumed that no matter what you do, just do something that you are allowed and enjoy. However, patients with low compliance may be more prone to poor adherence to general advices and a tailored exercise training program might be more effective than those unsupervised, as was shown in patients suffering from obsessive-compulsive disorder<sup>92</sup> and depression.<sup>93</sup> Hospitalized patients are certainly more manageable, and optimal results may be achieved in a short time, as was shown after 4-month prescriptions in schizophrenic patients.<sup>94</sup> To the extent that people have preferences for specific exercises, it is important to understand whether different combinations of specifiers could be equally beneficial for the patients, who

should conceivably be able to choose their favorite sport, or whether it would be better to focus on certain forms of exercise to avoid. In fact, despite various benefits of sport participation may be attained, such as the opportunity to overcome challenges or to fulfill basic psychological needs, there is a dark side of sport, ranging from injuries to addictions.<sup>95,96</sup> Patients with displeasure of body image or fear of gain in body weight should be carefully accompanied through mild exercise interventions, as compensatory behaviors may be present.<sup>29</sup> As stated by the guidelines, when subjects suffering from specific conditions are not able to meet the key recommendations of guidelines, they should still be engaged in regular physical activity according to their abilities, avoiding sedentary behaviors. Contrarily to the Mediterranean pattern,<sup>44</sup> to increase structured physical activity levels in the gym may be not affordable for high costs, but routine tips to make more movement are available (<https://www.choosemyplate.gov/physical-activity-tips>). To keep a daily active lifestyle, patients should make tricks to increase physical activity at home, at work, at school, in the community (eg, park the car away from the workplace, get off public transport a few stations before). Generally, little structured physical activity is much better than too much and unfocused, and sports with teammates are always preferable to individual sports.

## Sleep in Neuropsychiatry

Sleeping is a neurobiological state that occupies about 30–35% of our entire lifespan (7–8 hrs/night), being an essential behavioral factor for human life that is affected by environment, technology, and our 24/7 society.<sup>97</sup> Post-industrialized sleep hygiene is different from sleep of hominin ancestors, primarily attributed to changed sleep environment (ie, sleep site) that includes photoperiod, thermal stress, noise, sociality, and familiarity of surroundings.<sup>98</sup> However, sleep states are conserved across diverse animal species, possibly because of their brain-stem-dependence (highly conserved among vertebrates), in turn suggesting that sleep drives a common benefit to animal survival, which seems to be also related to the clearance of brain metabolites.<sup>99</sup> As we mentioned earlier, brain activity is constant and it primarily depends on the level of arousal, with a totally different pattern around day and night cycle. During the night, sleep cycles between two distinct states: the Rapid Eye Movement (REM) sleep, which occurs with vivid dreams, and the non-REM sleep, which occurs after sleep onset, both stages being

distinguished through electroencephalogram or electro-myogram. An imbalance between the two sleep states represents an early symptom of various neuropsychiatric disorders, suggesting that both sleep states have important roles.<sup>100</sup>

We mention that healthy eating and physical activity are worth promoting in patients affected by neuropsychiatric conditions, but we argue sleep hygiene is the third player of this triad to be promoted in terms of good quality and quantity. The compromising neurobehavioral performance resulting from poor sleep might indeed induce neuropsychiatric symptoms in healthy subjects and worsen the condition of affected subjects, therefore deeming necessary to consider also this aspect in clinical practice. In the following paragraphs, we discuss and describe: I) the reciprocal relationship between sleep and neuropsychiatric disorders, II) existing methods to assess sleep, III) practical suggestions to promote sleep hygiene.

## The Reciprocal Relationship Between Sleep and Neuropsychiatric Disorders

Sleep acts as a mediator of cognition, mood, and emotional memory<sup>101</sup> and, therefore, poor sleep hygiene is associated with worse mental health in both adolescents and adults. In healthy youths, short weekday sleep duration was associated with increased odds of mood, anxiety, substance use, and behavioral disorders.<sup>102</sup> Both poor sleep quantity and quality (ie, insomnia) are associated with worse mental health. For instance, short sleep durations are known to be a significant predictor of developing depression during adulthood<sup>103</sup> and subjects with insomnia are almost 10 or 17 times more likely to develop a depressive disorder or an anxiety disorder than good sleepers.<sup>104</sup> Sleep disorders have been intertwined with concomitant neuropsychiatric conditions<sup>105</sup> and different sleep structures can differentiate the clinical phenotypes, for instance between bipolar disorder and attention-deficit hyperactivity disorder.<sup>106</sup> Indeed, laboratory-based studies have demonstrated that sleep abnormalities are commonly present in affective disorders since years.<sup>107,108</sup> However, sleep disturbances still represent a growing public health concern, affecting youths and older adults suffering from neuropsychiatric diseases. About 88% of children with anxiety disorders exhibits sleep disturbances<sup>109</sup> and main complaints in adults suffering from Alzheimer's disease include fragmentation of nocturnal sleep, prolonged awakenings, REM sleep abnormalities, and daytime sleepiness

with frequent napping.<sup>110</sup> Sleep may be disturbed in some patients with obsessive thoughts that prevent them from falling asleep.<sup>29</sup> Sleep disturbances are also present in patients with bipolar disorder<sup>111</sup> and even non-treated schizophrenic patients,<sup>112</sup> clearly demonstrating that sleep is directly affected by the disease rather than drugs themselves. Interestingly, the clinical response to a specific drug therapy may be predicted by the cellular circadian rhythms in some patients.<sup>113</sup> Indeed, circadian rhythm disturbances may be one of the key etiological factors for neuropsychiatric disease onset, as they are frequently present in children diagnosed with attentional or hyperactive symptoms<sup>114</sup> and in older adults suffering from dementing disorders.<sup>115</sup>

## Existing Methods to Assess Sleep

Sleep quality, quantity, timing (fractal or condensed), and environment are four features that characterize sleep hygiene. As happens for eating patterns, quality appears to be the most important, because of its comprehensive annexation with efficiency (ie, time in bed spent sleeping), latency to fall asleep, and time in bed spent awake at night (we assume to have diurnal behaviors) after first falling asleep. Sleep behavior can be studied through several objective methods, such as polysomnography and actigraphy, or subjective methods, such as the more practical sleep diaries. Polysomnography refers to the continuous monitoring of multiple neurophysiological and cardiorespiratory variables over the night course<sup>116</sup> and specifically provides information about physiological changes occurring in relation to sleep stages and wakefulness.<sup>117</sup> The reference for the evaluation (<https://aasm.org/clinical-resources/scoring-manual/>) comprehensively provides rules for scoring sleep stages, arousals, respiratory events during sleep, movements during sleep and cardiac events, but it may be of limited use for clinical routine. Of note, existing recommendations for a good sleep hygiene focus on the sole quantity factor. The hours of sleep per night should be at least eight and seven for healthy adolescents<sup>118</sup> and adults,<sup>119</sup> respectively. Failing to meet these recommendations is associated with poorer physical health in youths<sup>120</sup> and adults.<sup>121</sup> Overall, almost one third of adults in the US sleep less than 7 hrs in a 24 hr period.<sup>122</sup> Furthermore, sleep quality seems to be far from being optimal with insomnia being one of the most prevalent health problems related to sleep. Insomnia is a chronic condition with difficulties in initiating and maintaining sleep that occurs in approximately 9–15% of the world population with daytime

consequences.<sup>123,124</sup> Dietary supplements to alleviate insomnia symptoms are used in about 15% of cases,<sup>72</sup> potentially exposing to drug–food interactions.<sup>58,125</sup> Despite not being the gold standard method for sleep monitoring, actigraphy can certainly represent a useful alternative and many scientific studies have been conducted with this objective method in different settings.<sup>126,127</sup> Actigraphy devices worn on the wrist record movements that can be used to estimate total sleep time and wakes after sleep onset.<sup>128</sup> Since decades, the American Academy of Sleep Medicine highlighted actigraphy as a valid and cost-effective method for diagnosing insomnia, circadian rhythm disorders, or excessive sleepiness.<sup>129</sup> Other practical tools are sleep diaries and questionnaires, which quantitatively summarize the individual's perception of sleep, and can easily be used to monitor the behavioral treatment of sleep disorders.<sup>130</sup> Sleep questionnaires are filled in once, while sleep diaries are filled in over a period of time, thus underscoring the greater amount of information recorded by the latter. Similar to dietary or physical activity questionnaires, sleep questionnaires are influenced by different sources of bias and inaccuracy, but their subjectivity does not necessarily provide inaccurate results. Since many sleep questionnaires, scales, and diaries have been validated and proposed<sup>130</sup> and since their primary outcome can be extremely different (eg, sleep quality or daytime sleepiness), the selection of a questionnaire should be based on the purpose of each specific study or clinical question. A recent study by Ibanez and colleagues<sup>81</sup> created and provided a public repository where all sleep diaries and questionnaires can be downloaded (<http://users.dsic.upv.es/~jsilva/Sleep/>).

## Practical Suggestions to Promote Sleep Hygiene

A cognitive-behavioral sleep intervention was able to ameliorate self-reported indices of sleep, daytime sleepiness, anxiety, and depression in adolescents with higher levels of anxiety and depressive symptoms.<sup>131</sup> The treatment of sleep-wake alterations in older adults with dementing disorders may provide immediate benefits on neuropsychiatric symptoms.<sup>132</sup> Light, as the main environmental modulator of the biological clock, is able to resynchronize the circadian system and bright-light therapy is currently proposed for the treatment of seasonal affective disorder, and in cases of non-seasonal depression, and bipolar depression.<sup>133</sup> In clinical practice,

actigraphy represents the more practical method to detect activity-rest circadian rhythms disorders in patient's natural sleep environment.<sup>134</sup> Nevertheless, sleep diaries and questionnaires should be always used to complement the objective evaluations. As mentioned for the dietetic sessions, sleep hygiene education may be more concrete with the support of written information. Generally, behaviors that augment physiological or mental arousal, or which delay the circadian phase, should be avoided. For instance, the consumption of methylxanthine-containing beverages, such as coffee, tea, and guarana should be avoided close to bedtime. Also, smoking should be avoided because of its insomnia-like sleep impairments,<sup>135</sup> but also alcohol.<sup>29</sup> Indeed, sleep may be indirectly favored by the abovementioned dietary and physical activity interventions, but patients may take prescribed or over-the-counter sleeping aids, such as melatonin.<sup>136</sup> Neuropsychiatric patients should be educated to ensure that their sleep environment is relaxing (eg, no light or noise, comfortable bed), by also limiting the use of mobile phones and television during bedtime. Concomitantly, patients should keep an active lifestyle (regular moderate-intensity aerobic exercise),<sup>137</sup> avoid heavy food close to bedtime,<sup>138</sup> avoid sugar-sweetened or energy beverages,<sup>139–141</sup> and possibly follow a tailored sleep plan or even use actionable resources, such as apps that promote sleep self-monitoring.<sup>142</sup>

## Conclusion

The medical-surgical world is increasingly oriented towards drug- or surgeon-centered treatments. Obesity is treated with anti-obesity medications or bariatric surgery,<sup>143,144</sup> insomnia with transcranial magnetic stimulation,<sup>145</sup> and treatment-resistant conditions with neurosurgical implants.<sup>146</sup> It seems that multiple benefits deriving from healthy diet, physical activity, and restful sleep have been progressively forgotten. The impending global pandemics of obesity and sleep disturbances are not effectively controlled by lifestyle interventions because the integration in clinical practice has never been systematic. Neuropsychiatric patients were often reported to have unhealthy dietary habits,<sup>27,34,147,148</sup> sedentary behaviors,<sup>77–79</sup> and poor sleep hygiene.<sup>109–112</sup> Even if some neuropsychiatric conditions can directly or indirectly affect eating behaviors,<sup>29</sup> in terms of direction of causality, a poor diet has remarkably been shown to precede the onset of mental illnesses,<sup>149</sup> with similar time dependence for both sedentary lifestyles and poor sleep.<sup>150,151</sup> Our suggestions, proposed in Table 1, may be applied to the general



**Table 1** Considerations for Clinical Practice Regarding Single Determinants of Healthy Eating, Physical Activity, and Sleep Hygiene (HEPAS) in Patients at Risk for or with Neuropsychiatric Disorders

<p><b>Healthy eating in neuropsychiatry practice</b></p> <ul style="list-style-type: none"> <li>• Do not skip breakfast</li> <li>• Avoid sugar-sweetened beverages</li> <li>• Eat complex carbohydrates (eg, whole grain pasta, rice, or bread) more than once a day</li> <li>• Eat vegetables and fruits more than once a day, following seasonality</li> <li>• Rotate second courses with meat, fish, legumes, dairy products, or eggs</li> <li>• Prefer vegetable oils (eg, olive oil) other than animal fats, such as butter or lard</li> <li>• Avoid fast-food (eg, hamburger) restaurants, commercially baked goods, pastries, sweets</li> <li>• Avoid unnecessary dietary supplements, which may cause drug-nutraceuticals interactions</li> <li>• Do not eat excessively</li> <li>• Try to eat always at the same hours</li> <li>• Share meals with family members or friends</li> </ul>
<p><b>Physical activity in neuropsychiatry practice</b></p> <ul style="list-style-type: none"> <li>• Keep an active lifestyle to achieve over 150 mins of moderate-intensity aerobic exercise per week</li> <li>• Adopts tricks to increase physical activity at home, at work, at school, in the community (eg, park the car away from the workplace, get off public transport a few stations before)</li> <li>• Do sports that you are allowed to do and that you enjoy</li> <li>• Little structured physical activity is much better than too much and unfocused</li> <li>• Do physical activities not close to meals or bedtime</li> <li>• Move with family members or friends</li> </ul>
<p><b>Sleep hygiene in neuropsychiatry practice</b></p> <ul style="list-style-type: none"> <li>• Sleep at least 7 hrs per night, avoiding unnecessary daytime naps</li> <li>• Try to go to bed and wake up always at the same hours</li> <li>• Limit the use of mobile phones and television during bedtime</li> <li>• Make sure that the sleep environment is relaxing (eg, no light or noise, comfortable bed)</li> <li>• Do not sleep excessively: a good nap is better than a bad sleep</li> <li>• Avoid heavy food or strenuous physical activity close to bedtime</li> <li>• Avoid methylxanthines (eg, coffee, tea, guarana, energy drinks), smoking, or alcohol</li> </ul>

neuropsychiatric population, with no regard for age, gender, or ethnicity. Public and private clinics, university hospitals, and research facilities are encouraged to integrate HEPAS, in order to pursue better course and outcome compared to related standard of care.

## Disadvantages, Barriers, Advantages

In Neuropsychiatry, routine screening of eating behaviors, physical activity levels, and sleep patterns are not always

accurate, mostly due to packed schedules or growing case-loads that prevent proper multidisciplinary interactions between neuropsychiatrists, nutritionists, and exercise trainers. HEPAS applicability may also be limited according to patient's severity/stage of disease and resource availability (eg, financial burden, lack of specialized personnel). Moreover, all three factors are quite onerous to monitor (weak point = low compliance) and patients are not often informed enough, hyperinformed (which may be probably worse), uneducated, and socially unengaged.<sup>152,153</sup> However, HEPAS epitomizes the novel approach that accounts for modifiable factors not only to ameliorate the grueling years lived with disability after diagnosis through tertiary preventive interventions, but also to avoid complications of clinical spectrum or to reduce disease onset through primary preventive interventions. HEPAS may certainly account for other non-communicable disease associated with the longest years lived with disability, such as musculoskeletal disorders (ie, osteosarcopenia in older adults with mild cognitive impairment), diabetes, kidney and cardiovascular diseases that are often comorbid with neuropsychiatric disorders.<sup>154,155</sup> Single HEPAS components were reported to provide various advantages also in neuropsychiatric populations, but no study ever investigated all of the three components.

## Past Evidences

HEPAS determinants are exceedingly intertwined, so that one cannot be dissociated from another. The combination of healthy eating and right amount of physical activity was observed to have multiplicative effects on mortality risk reduction.<sup>156</sup> The worse a subject eat the less active he is, and that was confirmed for both children and adults.<sup>157,158</sup> Moreover, youths who sleep little may be more prone to fast food consumption and vegetable or fruit avoidance,<sup>140</sup> with late sleep timing being associated with increased consumption of energy drinks, sugar-sweetened beverages, and breakfast skipping.<sup>139</sup> These associations may be due to changes in appetite regulatory hormones that subsequently contribute to overeating and obesity.<sup>159,160</sup> Conversely, eating habits can influence sleep through gut microbiota modulation.<sup>161</sup> Staying active is clearly better because it ameliorates sleep quality<sup>162</sup> and mood<sup>163</sup> not only in youths, but also in adults and elderly in turn providing a more resting sleep.<sup>164</sup> Regular physical activity has also positive effects on sleep quantity,<sup>165</sup> and the amelioration of sleep habits is in turn associated with a general risk reduction for obesity, heart diseases, and

diabetes,<sup>166</sup> which are conditions often being counted among the long-term metabolic side effects of neuropsychiatric drugs. Previously, some authors already acknowledged this concept of reciprocity among apparently disconnected domains, and advocated interventions targeting multiple factors simultaneously rather than focusing on single components. Similarly to HEPAS, a past multidomain lifestyle-based intervention provided ample evidence about the importance of coupling nutritional advices, exercise, and mental training for cognitive decline prevention.<sup>167</sup> In the same field, other trials targeted disease onset reduction through support in chronic disease management, smoking cessation, and health coaching.<sup>168</sup>

## Future Directions

We support the integration of HEPAS as central determinant in the prevention and multimodal approach of neuropsychiatric disorders, thus ultimately encouraging multidisciplinary interactions between specialists and researchers. Conceivably, high quality and adequately powered clinical trials should investigate HEPAS into diverse settings and disease populations in order to take full advantage of these behavioral interventions. In particular, there is the need of prospective experimental studies with an appropriate research methodology to legitimately support the beneficial effects of dietary,<sup>169</sup> exercise,<sup>170</sup> and sleep programs as primary or secondary prevention initiatives. Both youths and adults should be included in interventional studies, being the



## Healthy Eating, Physical Activity, and Sleep hygiene (HEPAS)

The winning triad for sustaining physical and mental health in patients at risk for or with neuropsychiatric disorders

**Steering group:**  
Matteo Briguglio, Mauro Porta, Bernardo Dell'Osso, and Ira David Glick.

### Adopt a healthy and balanced diet

- Diet quality: consume a proper food variety
- Diet quantity: do not eat excessively
- Food timing: try to eat always at same hours
- Food environment: share meals with family/friends

### Keep in touch with doctors

- Undergo periodic health screenings
- Maintain a high adherence to the pharmacological therapy
- Avoid unnecessary dietary supplements
- Feedback your doctor about doubts and concerns

### Get enough resting sleep

- Sleep quality: a good nap is better than a bad sleep
- Sleep quantity: sleep enough, but not too much
- Sleep timing: try to maintain bedtime at same hours
- Sleep environment: prep bedroom to aid sleep

### Stay daily active

- Physical activity quality: do what you are allowed to do
- Physical activity quantity: try to move every day
- Physical activity timing: move not close to meals or bedtime
- Physical activity environment: move with friends/family

We support the integration of HEPAS as central determinant in the prevention and multimodal approach of neuropsychiatric disorders, thus ultimately encouraging multidisciplinary interactions between specialists and researchers. Conceivably, clinical trials should investigate HEPAS into diverse settings and disease populations in order to take full advantage of these behavioral interventions. Both youths and adults should be included in interventional studies. Real-world approaches to promote healthy habits, enhance physical activity, and increase sleep quality should be investigated, being social engagement the common denominator.

**Figure 1** Scholarly infographic depicting the Healthy Eating, Physical Activity, and Sleep hygiene (HEPAS) in patients at risk for or with neuropsychiatric disorders.

research on adolescent populations even more important because of the negative trend towards adulthood for healthy eating,<sup>171</sup> physical activity,<sup>172</sup> and sleep.<sup>173</sup> Real-world approaches to promote healthy habits, increase sleep time, and enhance physical activity should be investigated, being social engagement the common denominator. Patients should be ultimately confident, motivated, and enabled to sustain long-term health outcomes. Infographic of Figure 1 comprehensively summarizes our considerations for clinical practice, also comprising advices on a proper therapeutic alliance. Importantly, caregivers and family members should always be involved in this multimodal approach to practically and psychologically support the individual. If necessary, psychotherapists and life coaches may be involved to enhance compliance and community-based engagement.<sup>152</sup> We know all positive effects of abovementioned HEPAS interventions, but for instance, how does an individual eat better, sleep better, and do exercise? Since each component can provide various advantages per se, the possibility of combined use of all three interventions unlocks numerous potential avenues, facilitating a comprehensive management of neuropsychiatric disorders in affected patients.

## Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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