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Highlights

- Ketogenic diet improved mood including calmness, contentedness and alertness compared to other diet controls
- Individuals on ketogenic diet are less anxious and depressed compared to other diet controls
- Cognitive and emotional stress is lower in individuals on ketogenic diet compared to other diet controls
- Participants following a ketogenic diet are less lonely compared to other diet controls

Ketogenic Diet has a positive association with mental and emotional well-being in the general population

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Abstract

Ketogenic diet reduces pathological stress and improves mood in neurodegenerative and neurodevelopmental disorders. However, the effects of ketogenic diet for people from the general population have largely been unexplored. Ketogenic diet is increasingly used for weight loss. Research in healthy individuals primarily focuses on the physical implications of ketogenic diet. It is important to understand the holistic effects of ketogenic diet not only the physiological but also the psychological impacts in non-clinical samples. The aim of this cross-sectional study with multiple cohorts was to investigate the association of ketogenic diet with different aspects of mental health including calmness, contentedness, alertness, cognitive and emotional stress, depression, anxiety and loneliness in a general healthy population. Two online surveys were distributed: *Cohort 1* using the Bond-Lader visual analogue scale (BL-VAS) and Perceived Stress Scale (PSS-10) (n=147) and *Cohort 2* the Depression, Anxiety and Stress Scale (DASS-21) and UCLA-R Loneliness scale (n=276). Ketogenic diet was associated with higher self-reported mental and emotional well-being behaviours including calmness, contentedness, alertness, cognitive and emotional stress, depression, anxiety and loneliness compared to individuals on a non-specific diet in a general population. This research demonstrated that ketogenic diet has potential psychological benefits within the general population.

Keywords

Ketogenic diet, mood, cognitive and emotional stress, depression, anxiety, loneliness, calmness, contentedness, alertness

Introduction

Ketogenic diet, a high fat, moderate protein and low carbohydrate diet, is a nutritional therapeutic fasting diet altering the body's metabolism from glycolysis to fatty acid utilisation, providing the body and brain with an alternative fuel source to glucose [1]. Ketogenic diet has been used safely and effectively for over 100 years for the treatment of childhood refractory epilepsy [1]. Ketogenic diet has been clinically trialled in neurodegenerative diseases, such as Alzheimer's disease [2] and multiple sclerosis [3] and in neurodevelopmental conditions, such as anxiety, depression [4-7] and schizophrenia [8-11] (comprehensive reviews [1, 12]). However, the effects of ketogenic diet on the general population are not well studied.

Ketogenic diet is increasingly used by the general population, with around 7% of Americans following a ketogenic lifestyle in 2022, captured using an online survey of 1005 Americans aged 18-80 [13]. Similarly, a UK keyword analysis study in 2021 found that ketogenic diet was the second highest, with 300000 average monthly searches, search term [14]. In addition, the hashtag "keto" appeared on Instagram in over 21 million posts during the same time period [14]. Reasons for starting a ketogenic diet are mostly physiological, such as weight loss [15], type I & II diabetes [16, 17], as an experimental treatment for mental health conditions (comprehensive reviews [1, 12]) or cardiovascular diseases, cancers [18], brain trauma [19] and migraines [20] (comprehensive reviews [21, 22]). However, general well-being requires a holistic interplay between physiology and psychology. Most research to date in the general population has investigated the physiological benefits and side-effects of the ketogenic diet [15] while overlooking the potential psychological implications.

Good psychological health is essential for all aspects of everyday life including overall well-being, ability to work and relationships [23]. The global burden of mental health disorders significantly increased from 80.8 million disability-adjusted life-years to 125.3 million between 1990 and 2019 [24]. Around 7.2% of the world's population are currently living with symptoms of anxiety and depression, both with and without a formal diagnosis [23]. Around, 1 in 6 English adults meet diagnostic criteria for mood disorder, yet only 1 in 8 of these adults receive any kind of treatment [25]. These figures suggest a degree of unmet clinical needs and obfuscate the real-world burden of disease conferred by affective disorders. Chronic stress is a precursor of mental illnesses such as neurodegenerative and neurodevelopmental disorders [26, 27]. Stress is a response to physical and psychological demands [28]. Chronic stress causes 'wear and tear' on neural cells [29] leading to progressive neurocognitive dysfunction and pathology [30]. Changes in diet may assist in mitigating not only the physiological effects of affective disorders and stress, but also alleviate psychological symptoms. Therefore, it is vital to understand not only the physical implications of ketogenic diet in the general population, but also its association with mental health. More effective treatments and preventions for mental health disorders are needed, particularly for those with subclinical symptoms who may not seek or qualify for formal help.

The increased use of ketogenic diet in the general population creates the need to investigate the association of ketogenic diet with mental and emotional well-being. Here, we aimed to investigate the relationship between ketogenic diet and mood (calmness, contentedness, alertness), depression symptoms, anxiety symptoms, loneliness and cognitive and emotional stress in the general population. We hypothesised people from the general population following the ketogenic diet will have more positive mood, lower

depression and anxiety symptoms, lower loneliness and cognitive and emotional stress, than those not following the diet.

Methods

Participants

Multiple participant cohorts were recruited as part of two studies receiving ethical approval from Northumbria University Research Ethics Committee (Cohort 1: 26063, Cohort 2: 29625) and were conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants prior to collecting their data.

Participants were recruited using opportunity sampling though social media platforms. Cohorts had the same inclusion and exclusion criteria. Participants had to be 18 years of age; we did not specify a particular age range as this study was an exploratory study to understand the current population consuming ketogenic diet. Exclusion criteria applied to individuals with pre-existing clinically diagnosed mood, anxiety disorders, neurodevelopmental and neurodegenerative conditions. Individuals following a ketogenic diet had to have adhered to the lifestyle for at least 1 week. Participants were recruited for Cohort 1 between February 2021 to October 2021 for Cohort 2 between January 2022 to July 2022.

Using *a priori* G*Power analysis [31] for both cohorts showed that the minimum sample size necessary to achieve 80% statistical power with a T-test/Mann-Whitney test was calculated as 134 participants; 67 in a ketogenic diet group, 67 in a non-ketogenic diet group, assuming $d = .5$ and $\alpha = .05$ per cohort.

Measures

All Participants

Demographics & Socioeconomic questions

Demographic, socioeconomic and health information were collected, including age, gender, country of residence, ethnicity, level of education, employment status, accommodation status, height, weight, subjective health rating, diabetes diagnosis, high blood pressure or a blood pressure diagnosis.

Dietary Questions (Ketogenic diet and Other diet)

Dietary habits of all participants were assessed using the short-form food frequency questionnaire (SFFFQ) [32]. Participants were asked to reflect on their usual food consumption across a week. This questionnaire SFFFQ has shown significant agreement with the longer food frequency questionnaire and 24-hour dietary recall [32].

In addition, all participants were asked if they currently followed a Ketogenic diet.

Ketogenic diet participants were asked to provide length of lifestyle followed, primary reason for ketogenic diet and type of ketogenic diet. Participants who followed a ketogenic diet were also asked if they measured their levels of ketone bodies, if so, how and what their last reading was.

Where participants did not follow a ketogenic diet (other diet), they reported if they followed a different diet type, length of alternative lifestyle followed, any allergies, importance of healthy eating and definition of healthy eating. Some of these questions were not included in the analysis rather they aided in ensuring that all participants completed equal amounts of questions.

Cohort 1

Perceived Stress Scale (PSS-10)

The Perceived Stress Scale (PSS-10) has been validated for investigating general perceptions of stress (cognitive stress) and its relationship to pathology and behaviour [33]. Ten questions assessed thoughts and feelings over the last month, scored on a Likert scale from 0 (i.e., never) to 4 (i.e., very often). Total PSS-10 score ranges from 0-40 (Low stress: 0-13, Moderate stress: 14-26, High perceived stress: 27-40) [33] (‖ = .89).

Bond-Lader Visual Analogue Scales (BL-VAS)

Bond-Lader Visual Analogue Scales (BL-VAS) [34] captured current mood for a series of 16 opposing mood pairs (e.g., Alert – Drowsy). A sliding scale from 0-100 indicated level of current mood for 16 opposing mood pairs [35]. Reliability analysis indicated excellent reliability for alertness (‖ = .93), contentedness (‖ = .88) and low reliability for calmness (‖ = .52).

Cohort 2

Depression, Anxiety, Stress Scale (DASS-21)

The DASS-21 [36] comprises 21 items split into three 7-item subscales that measure depression (D), anxiety (A), and emotional stress (S). Participants respond on a four-point severity scale (0 = never, 1 = sometimes, 2 = often, 3 = almost always) [36]. There are standard cut offs for each subscale to indicate severity from normal (D: 0-9, A: 0-7, S: 0-14), mild (D: 10-13, A: 8-9, S: 15-18), moderate (D: 14-20, A: 10-14, S: 19-25), severe (D: 21-27, A: 15-19, S: 26-33), or extremely severe (D: 28+, A: 20+, S: 34+). The DASS-21 is rated as having excellent or very good reliability for depression (‖ = .91), anxiety (‖ = .84) and stress (‖ = .88).

Discussion

The present study aimed to investigate the differences between people in a general population currently participating in a ketogenic diet to those who were not, on calmness, contentedness, alertness, cognitive and emotional stress, depression, anxiety and loneliness. We hypothesised that people following ketogenic diet would have a more positive profile on all outcome variables, based on findings demonstrated in clinical populations [12]. We found that people following ketogenic diet had a significantly better psychological well-being including calmness, contentedness, alertness, stress, depression, anxiety and loneliness in a general population (Table 4). These differences remained for all measures except for loneliness when we controlled for identified group differences. Within a small sub population, we identified that length of ketogenic diet relates to mood and stress, whereas level of ketosis did not have a significant relationship to the previous dependent variables. Control participants were following various diets so no one diet received over representation amongst the comparison participants.

Table 4: Summary results describing the changes with ketogenic diet compared to other diet participants.

Measure	Behaviour	Differences with Ketogenic diet
Bond Lader Visual Analogue Scale	Alert	↑
	Content	↑
	Calm	↑
Perceived Stress Scale	Stress (cognitive)	↓
Depression, Anxiety, Stress Scale	Depression	↓
	Anxiety	↓
	Stress (emotional)	↓
Loneliness	Loneliness	↓

Ketogenic diet has been described as a diet which “calms the schizophrenic mind” [43], this study demonstrated that ketogenic diet poses this calming effect beyond the clinical sample and beneficial differences can be extrapolated to the general population. A case study demonstrated that a gluten-free, casein-free ketogenic diet increased calmness in a child with epilepsy and autism [5]. Similarly, a case report stated that a female with bipolar disorder (II) on ketogenic diet felt calmer and more confident [44]. Glutamate is the main excitatory neurotransmitter within the brain with the counterpart being Gamma-aminobutyric acid (GABA) acting as an inhibitory neurotransmitter [45]. Ketogenic diet might be sharing similar mechanism with alprazolam, commonly used to treat anxiety disorders [46], by increasing GABA and creating calmness and relaxation/content [46]. The effects of ketogenic diet on GABA are controversial, as some studies show an increase of GABA with ketogenic diet [47, 48], and, some a decrease [49] (for full review see Kraeuter, Phillips [12]). Therefore, increasing GABA availability could be the potential mechanism by which ketogenic diet might have emotion regulation effects. Further research is needed to investigate if GABA increases with ketogenic diet in a general population.

In addition, in this study ketogenic diet was associated with positive alertness, as demonstrated within this study, and shown previously in patients with epilepsy (reviewed by van Berkel, DM [50]). This review demonstrated 15 studies investigating alertness, including 533 patients, 51.5% reported an increase in alertness [50]. Not all studies found higher alertness to be significant [51]. This suggests that rather than ketogenic diet inducing a flat emotional state, arousal levels are balanced to ensure that people are emotionally regulated and appropriately attending to their environment.

Contrary to previous literature [50], we found that length of time on ketogenic diet was positively correlated with calmness, contentless or alertness. Previous literature found shorter treatment increments with ketogenic diet (up to three months) and longer interventions found comparable results [50]. Within our study, we investigated a wide spread of length of ketogenic diet compared to previous literature investigating broader time spans less than 3 month and more than 3 months. Our findings suggest that mood benefits increase the longer individuals remain on the diet. Future studies with larger sample sizes could consider whether the relationship between length of time on ketogenic diet and emotion regulation effects are non-linear in nature. Rather than reflecting a standard linear relationship, it may be that people need to adhere to the diet for a specified period before the benefits on mood and arousal can be realised. Investigating this critical time window could assist in understanding the mechanism which is underpinning the effects of ketogenic diet on neurotransmitters such as GABA.

Stress is an important modulator/precursor to many psychiatric illnesses and therefore reducing stress might delay onset of disease or reduced disease severity for both physical and mental health disorders [26, 27]. Here, we demonstrated that people following the ketogenic diet had lower perceived stress/cognitive stress using the PSS-10 in cohort one and the stress scale measures by the DASS/emotional stress in cohort two. This provides robust, corroborative, cross cohort evidence that ketogenic diet reduced cognitive and emotional stress within a healthy general population. We also identified that individuals longer on ketogenic diet had lower cognitive and emotional stress. All individuals regardless of diet were categorised within the normal stress category; however, ketogenic diet

individuals were scoring in the middle of the normal stress category and other diet participants bordered on mild stress. The primary biomarker for stress is cortisol [52]. Eight weeks of a very low-calorie ketogenic diet reduced salivary (acute) cortisol in obese male population [52]. Four weeks of ketogenic diet reduced acute cortisol measurements [53]. Contrary, another study found that serum cortisol concentrations (acute) were increased with ketogenic diet compared to baseline levels [54]. Indicating that ketogenic diet influences the hypothalamus-pituitary-adrenal (HPA) axis by altering cortisol concentrations to maintain homeostasis [52]. Increased GABAergic neurotransmission, as seen with ketogenic diet, results in inhibition of the HPA axis by inhibiting neurons within the paraventricular nucleus reducing the secretion of adrenocorticotropic hormone, resulting in reduced cortisol release by the adrenal glands [55].

Most studies to date have investigate salivary or blood cortisol [52, 53] measurements assessing the acute state of cortisol at collection of the sample. Using acute measurement techniques such as saliva and blood has its limitations due to intra- and inter- day variations [27]. We are not aware of studies investigating cortisol concentrations in hair sample, which will aid to understand the retrospective long-term impact of ketogenic diet on chronic cortisol concentrations. Therefore, it would be beneficial to assess cortisol in hair or nails [27] to understand the effects of ketogenic diet on chronic cortisol levels and its prolonged effects on HPA axis to help maintain homeostasis [27].

People following the ketogenic diet had significantly lower anxiety scores. Here, we found that individuals not on ketogenic diet were classed in the mild anxiety category, whereas individuals on ketogenic diet were classified as normal anxiety symptoms. Similarly,

ketogenic diet individuals were classified as normal on the depression scale, whereas non-ketogenic diet individuals were categorized as mildly depressed. These findings demonstrate that ketogenic diet has a positive association with symptoms of depression and anxiety in the general population. Previous studies have found similar results in preclinical and clinical settings. Preclinical mouse/rat models have shown a reduction in anxiety and depressive-like behaviours with ketogenic diet [56-60] (for full review[12]). Clinical setting include bipolar disorder [61-64], psychosis [62] and schizoaffective disorder [62] (for full review [48, 65, 66]). A study focusing on weight loss, physical performance, cognitive function and metabolic parameters, also investigated the effects of ketogenic diet on depression and anxiety, using the center for epidemiological studies depression scale and the state-trait anxiety inventory [54]. Twelve weeks of ketogenic diet reduced anxiety and depression scores, however, not significantly [54]. This difference might be due to length of diet as here individuals followed on average a ketogenic diet lifestyle for 44.02 ± 64.97 months. Supporting this hypothesis are our findings that length of ketogenic diet was negatively correlated with anxiety scores.

One underlying mechanism of major depressive disorder and anxiety disorder is reduced GABA neurotransmission [48], in turn creating calmness and relaxation [46]. As discussed earlier, ketogenic diet has been shown to alter GABAergic neurotransmission, which might be one potential pathway by which ketogenic diet modulated depressive-like and anxiety-like symptoms [47, 49] (for full review see [12]). In addition, current anti-depressant medications function by increasing the availability of other neurotransmitters such as serotonin and dopamine [67]. Ketogenic diet has been shown to increase dopamine and its metabolites in an animal model of Parkinson's disease [68]. In children with epilepsy, three

months on ketogenic diet significantly elevated dopamine and serotonin concentrations in cerebrospinal fluid, but ketogenic diet did not influence norepinephrine [69].

Humans have a drive for social connections and belonging [37], which is driven by a combination of an activation of the dopaminergic rewards circuits within brain regions, release of the neuropeptides oxytocin and vasopressin, stimulation of endorphin and endogenous opioid release [70]. Social isolation and feelings of loneliness can be stressful events [70]. Increased loneliness has been shown to be associated with increased HPA axis activity resulting in increased cortisol release [71-73]. Here, we found that ketogenic diet was associated with reduced perceived loneliness. Previous studies have demonstrated the pro-social effects of ketogenic diet in neurodevelopmental disorders such as ADHD [74] and ASD [5, 6, 75]. Pro-social behaviours have been associated with increased serotonin availability [76], oxytocin [77, 78], vasopressin, dopamine and endorphins [70]. On the contrary, glucocorticoids and corticotrophin releasing hormones are associated with reduced sociability [70]. As previously outlined ketogenic diet has been shown to alter cortisol concentrations [52], increase in dopamine [68, 69] and serotonin [69]. This result however did not remain significant when the demographic characteristics were considered. It is possible that as well as feelings of social connection being driven by psychobiological factors, such as diet, loneliness is also related to social demographic and economic factors such as those considered in the current study. Feelings of social defeat, which equally relate to psychological and social factors, may be as relevant to loneliness as the psychobiological. A more systematic study needs to consider the factors which could explain the initial differences between those on a ketogenic and non-ketogenic diet for loneliness. In future

studies, we should also investigate other social behaviours. Sociability is a complex construct of multiple individual behaviours, loneliness being one aspect, additional behaviours to investigate might include empathy, vocal and non-vocal communication.

Ketogenic diet is increasingly a lifestyle of choice for many individuals within the general population. Most studies to date have only investigated the effects of ketogenic diet in clinical populations or its impact on physiology. This study provides strong evidence for the psychologically safe and beneficial application of ketogenic diet in a general population.

Although investigating in a general population poses great advantages, it also provides its challenges and limitations. The cross-sectional retrospective design of the study limited our ability to assess the dietary profile in more detail. It would be beneficial to explore in future studies the influence of micronutrients such as fiber intake and polyunsaturated fatty acid intake. The SFFFQ is used to assess diet retrospectively and has significant agreement with the longer food frequency questionnaire and 24-hour dietary recall [32]. Currently, no food frequency questionnaire is designed to assess ketogenic diet. The SFFFQ was designed to assess the dietary quality based on UK regulations [32, 79]. Ketogenic diet does not follow current dietary guidelines and standards. Current UK guidelines state that a total of 50% of energy should come from carbohydrates, 35% from fat and 15% from proteins [79]. Contrary, a traditional ketogenic diet suggest that 70% of the daily energy is derived from fat, 20% from protein and only 10% from carbohydrates [22]. Therefore, the authors have provided a novel way of presenting self-reported ketogenic diet compliance but do acknowledge a degree of subjectivity regarding the classification. Nevertheless, the authors provided a detailed methodology of the adapted way of analysing the SFFFQ for ketogenic

diet purposes enabling future research to replicate or modify the protocol slightly. The only way to establish if a participant is following a ketogenic diet correctly is through the measurement of ketone bodies.

Most ketogenic diet participants did not monitor ketone bodies, these individuals may follow a ketogenic diet without being in a metabolic state of ketosis. A recent systematic review of ketogenic diet in epilepsy highlighted the need for more ridged monitoring of adherence to the diet [80]. The current study design did not allow us to provide means to measure ketone bodies. Future intervention studies should assess if self-reported ketogenic diet patters assess through the SFFFQ correlate with ketone levels. However, we were able to demonstrate using the SFFFQ that individuals on ketogenic diet follow a different dietary pattern to individuals not on ketogenic diet. The dietary pattern followed by individuals on ketogenic diet was in-line with what would be considered a traditional ketogenic diet.

The measures used within this study are highly validated self-reported measures. Contradictory research demonstrates potential reporting bias [81]. Recent study demonstrating that negative feelings might receive higher ratings [81], which could have potentially resulted in elevated mood scores, however regardless of potential self-reported measure bias dietary differences were observed.

We identified that ketogenic diet has a positive association with mental and emotional well-being measures such as calmness, depressive behaviours, anxiolytic behaviour and loneliness. We discussed that ketogenic diet might exert its behavioural benefits through modulating neurotransmitter availability and neuropeptides, endorphin, and endogenous opioid release. Our findings provide strong corroborative survey-based evidence that

ketogenic diet is effective in modulating cognitive and emotional stress. Future research should support these survey-based findings through biological evidence, as outlined above.

The gut microbiome might form the connecting link between diet and behaviour [82, 83]. During the symbiotic mutually beneficial relationship the gut microbiota consumes dietary components while producing neuromodulatory metabolites for the host organism [82, 83], including GABA, dopamine, serotonin and norepinephrine and their precursors [83]. Neurotransmitters are not able to cross the blood brain barrier, but neurotransmitter precursors produced by the gut microbiome can cross the blood brain barrier and are then converted to functional neurotransmitters to exert behavioural effects [83]. Gut autonomic nerves carry sensory information to the brain [82], which are activated by local metabolite stimulation [82]. The fecal microbiome encodes glutamate decarboxylase, which is the enzyme essential for converting glutamic acid to GABA [82, 84]. In addition, the gut microbiota influences the HPA axis [85], as germ free mice showed elevated corticosterone (mouse equivalent to cortisol) in response to restrain stress [85]. Recolonisation of the gut of germ-free mice resulted in reduced HPA axis activation [85]. In turn, ketogenic diet has been shown to alter the above neurotransmitters and their precursors, stress and the gut microbiome [86]. Therefore, the gut microbiome might be an additional mechanistic explanation for the behavioural changes seen with ketogenic diet in the general population. Further research is needed to establish the connections between behaviour, neurotransmitters, HPA axis activation, gut and brain function. It will be vital to control within these proposed studies for supplement usage such as pre/probiotics.

In conclusion, we demonstrated that individuals on ketogenic diet self-reported and confirmed by the SFFFQ showed more favorable self-reported behaviours including calmness, contentedness, alertness, cognitive and emotional stress, depression, anxiety and loneliness in a general population compared to individuals not following a ketogenic diet. Future studies should support these survey-based findings through biological evidence including the HPA axis and gut microbiome. This research has demonstrated that following a ketogenic diet has a positive association on mental health in the general population.

Author Contributions

Conceptualisation: Ann-Katrin Kraeuter and Emma Barkus

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Writing- review and editing: Sarah Garner, Evan Davies, Emma Barkus, Ann-Katrin Kraeuter

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Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declaration of interest statement

The authors have no conflict of interest to report.

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CRedit Author statement

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Declaration of Interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: