

RESEARCH ARTICLE

A 57-YEAR FOLLOW-UP INVESTIGATION AND REVIEW OF THE MINNESOTA STUDY ON HUMAN STARVATION AND ITS RELEVANCE TO EATING DISORDERS

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Abstract

Objective: This follow-up study reports on 19 of 36 male participants in the Minnesota Semi-Starvation Experiment. As systematic data were obtained for only 3 months of controlled nutritional rehabilitation following 6 months of semi-starvation, the follow-up aim was to re-examine the acute effects and inquire into possible long term physical and psychosocial effects from undergoing semi-starvation. The experiment has been a source of information for understanding eating disorders, particularly anorexia nervosa. Therefore, another aim was to examine the relevance of any starvation-induced symptomatic changes to eating disorders.

Method: Semi-structured phone interviews were employed to explore 1) physical and psychological consequences of semi-starvation and nutritional rehabilitation 2) eating and weight changes during and since completion of the experiment, and 3) quality of the participants' lives following completion of the experiment.

Results: Participants proceeded to lead interesting and productive lives, free of life-long adverse effects. Personality differences, inferred from the Minnesota Multiphasic Personality Inventory, likely influenced the severity of the psychopathological reactions to starvation. Many participants reported maintaining a higher than normal weight and had abnormal eating habits for many months and even years before returning to "normal" state.

Discussion: Reestablishment of normal body weight took significantly longer than suggested in the original experiment, and might therefore constitute a factor contributing to the extended course of illness and tendency to relapse in eating disorders. The preservation of energy and normal to high activity levels in the presence of signs of severe weight loss and starvation and body image disturbances seen in anorexia nervosa were not observed nor reported in the Minnesota Semi-starvation Experiment.

Keywords: semi-starvation, healthy volunteers, anorexia nervosa, eating disorders, MMPI

The Minnesota Experiment on the Biology of Human Starvation was carried out at the University of Minnesota in 1944/45 (1). It remains the most systematic, ethically justified study of experimental semi-starvation to date. The study was designed to monitor the physiological and psychological effects of severe and prolonged food restriction in 36 healthy young volunteer males, recruited from conscientious objectors during World War II. The experiment involved a 3 months baseline control period, 6 months of semi-starvation, and 3 months of controlled nutritional rehabilitation. The results were published in 1950 as “The Biology of Human Starvation” (1)

Researchers and clinicians have long regarded this wartime Minnesota semi-starvation study abbreviated from here on as the 'Keys study' as a source of information for understanding eating disorders (2-4). Our aims in conducting this essentially qualitative follow-up of the experimental subjects after 57 years were 1) to re-examine the acute, and inquire into possible long-term, physical and psychosocial effects from undergoing semi-starvation in these originally healthy volunteers; 2) to compare the data obtained from the participants to symptoms observed in eating disorder patients; 3) to obtain information on the participants' quality of life. The follow-up interviews were conducted in 2002, when most men were in their late 70's or early 80's.

1.1. The Semi-Starvation Experiment

Toward the end of World War II, Dr. Ancel Keys, well known for his invention of the “K ration”, and Dr. Josef Brozek collaborated with others from the Laboratory of Physiological Hygiene to design a scientific study on human semi-starvation. Their goal was to characterize psychological and physical consequences of starvation and explore “refeeding” strategies, thus permitting data-informed rehabilitation of food-deprived civilians and prisoners of war.

From over 100 volunteering conscientious objectors in the Civilian Public Service (CPS), 36 men were chosen to participate in the study. The inclusion criteria specified good physical and mental health, normal weight range, unmarried, the ability to get along well with others under difficult conditions, and a genuine interest in relief and rehabilitation work. Each applicant completed the Minnesota Multiphasic Personality Inventory (MMPI), which had just been published (5).

The average age of the 36 men who served as subjects was 25 (range 20-33) years. Physically, they were similar to their draftee peers, although slightly taller and relatively thinner than the average adult male in the US at the time. Unlike the draftees, 25/36 men belonged to the historic peace churches that rejected participation in combatant military service. They also differed intellectually and educationally from their peers in the army. All had at least one year of college, and 18 had college degrees (range of education was 13-19 years). Their IQ scores were almost identical with scores of a graduate class in advanced statistics at Columbia University. On the Army General Classification Test of IQ the 36 men averaged 2 SD above the mean for Selective Service inductees, equivalent to an IQ of 130. Thus, the participants represented healthy young men with an above average IQ.

During the 3-month control period, the men ate an individualized diet in order to achieve their ideal body weight according to height and activity level. The mean caloric intake per day during the control period was 3492 calories. The 6 months semi-starvation phase was designed to bring about a loss of 25% of their ideal body weight. Average caloric intake during this phase was 1570 calories. Mimicking the European wartime conditions, the diet included large amounts of cabbage and potatoes with minimal amounts of meat and dairy. Thirty-two men reached the goal of a 25% weight loss. Four subjects were

excluded from the study because they did not lose the expected weight. For the rehabilitation phase, the remaining 32 men were divided into 4 groups with food differing in caloric content in order to determine what effect the caloric content of food had on the rate of rehabilitation. After 3 months of controlled re-feeding, none of the men had reached their control weights. At this time, the men were allowed to eat an unrestricted diet and some of the men left the study. Twelve men remained in the experiment to be monitored for an additional 2 months. Twenty-one subjects were reevaluated eight months after the start of rehabilitation and 8 men were reevaluated at one year.

The men were required to continue or enroll in educational programs at the University and work 15 hours each week in study associated jobs. They were also encouraged to continue recreational and social activities according to their ability. Required exercise included walking 22 miles/week and 30 minutes/week of 10% grade walking on a treadmill. They were closely monitored throughout all phases of the study with frequent physical and psychological testing.

The Follow-up:

METHODS

2.1. Samples and Procedures:

The follow-up investigation was approved by the Institutional Review Committee of the University of Minnesota. "The Biology of Human Starvation" (1) listed the names of the men, but did not link them to their case numbers. One participant, contacted by the principal investigator, provided the addresses. Of the 36 participants, six participants could not be located and eleven were deceased. Of the 19 participants who were contacted, all agreed to participate in the follow-up. Our sample includes two out of four men who did not complete the study. Since one of the

eleven deceased participants had made a detailed videotaped interview about his experience in the study at the University of Colorado in 1990 (6), it was possible to include information about his extensive changes in eating behavior and weight.

2.2. Interviews and Data Review:

After obtaining informed consent, two of the investigators (EE and SS) completed interviews of the participants by telephone about their experiences during and following the original experiment. On average, interviews of participants lasted about 90 minutes. The interview was guided by a semi-structured questionnaire containing open-ended and specific questions and a checklist. Brief notes were added as the interview progressed. Each participant was questioned about the following topics: the personal history preceding participation in the original experiment including their psychological adjustment, physical health, and their weight and eating patterns. Participants were queried about their personal experiences and any psychological, physical, cognitive, and behavioral changes during the experiment. Each participant was systematically questioned about the following topics experienced during starvation: 1. energy level, lethargy, and fatigue. 2. food and eating-related changes 3. non-food related changes such as collecting things, smoking changes, chewing gum, and 4. cognitive changes. Each participant was asked whether or not they recalled feeling depressed versus non-depressed, and/or irritable. We specifically focused on changes in eating behavior and weight which occurred during and after the experiment in each participant. Several participants shared personal notes with us that they had kept during the course of the experiment. We explored the men's personal and professional lives following the experiment, and any abnormal eating and weight patterns and related physical and psychological issues.

RESULTS

3.1. Demographics and Career Outcomes:

The mean age of the 19 out of 36 participants at follow-up interview was 79 years with a range from 75 to 83 years. All men were college graduates, six had attained a Ph.D. and one an M.A. Six were college professors, four teachers, two ministers, an architect, a lawyer, an engineer, and a social worker. All felt they had led useful and interesting lives. Six attributed aspects of their vocational and avocational interests to their participation in the study. Ten indicated that their perceptions and perspectives regarding food were permanently altered by the study experience. All, but one, indicated they would participate again.

After the experiment ten men went on to help with world-wide relief efforts. One went on to give lectures on world hunger and his experience with starvation. Three men wrote books and received various awards, and six men travelled and worked in various parts of the world.

Max Kampelman is the best known of the study participants. He went on to a successful career in law, teaching, and politics, and eventually became a distinguished career diplomat, culminating in being awarded the Presidential Citizen's Medal in 1989 and the Presidential Medal of Freedom in 1999. His autobiography includes a description of his participation in the semi-starvation study (7). He entered the study with the same pacifist ideals as the others as a 24 year-old law student. Despite suffering the distressing physical consequences of semi-starvation including significant edema, lethargy, mild depression and irritability, he was able to finish law school and successfully took courses toward an MA in political science during the experiment.

3.2. Physical Changes:

Decades after participation, men recalled the prominent physical sensations and changes during semi-starvation described in the original study. They all recalled a gradual decrease in strength, coordination, and endurance, a sense of lethargy paralleled by a general curtailment of self-initiated spontaneous activities. Twelve men recalled they most dreaded the Johnson treadmill test, which involved walking on a treadmill until they felt they literally could not continue; two fell with total exhaustion on completion of the test. They avoided stairs and extra exertion whenever possible. One man stated "exercising was the hardest thing we did". None of the men interviewed reported periods of increased activity.

Although the Keys report states that physical symptoms gradually improved and the men were generally back to a normal physical state at 8 months, two participants stated that it took longer, in one case up to two years, to regain their former strength and stamina.

3.3. Eating Related Behavior During Semi-starvation:

The men confirmed the Keys report that food and eating and thoughts about and preoccupation with food became the earliest and most prominent focus and main topic of conversation. Five men recalled collecting recipes or cookbooks, ten reported distress about the waste of food, seven enjoyed the vicarious pleasure of watching others eat, while others tried to avoid watching others eat. Some reported dreaming about eating forbidden foods and waking up feeling guilty. During mealtimes, three reported creating odd concoctions with their food, while others added spices or additional water to their soup. Some ate more rapidly, while others dawdled over food and licked their dishes in order to get the last morsel of food. Ten drastically increased their consumption of coffee (up to 15 cups per day) and water in an attempt to

fight hunger. Fourteen men interviewed reported chewing gum, although not all to excess, and one man stated “we all chewed gum”. The Keys researchers reported that 4 participants chewed gum compulsively, up to 40-60 packs a day (8). Four men interviewed stated they began smoking.

One of our participants wrote in his personal diary: “Several of us got talking about how people play with their food...men paw over the food, shove it from one side of the plate to the other, spend gobs of time making sandwiches, continue to jump up and down fixing this and getting that.”

Four men recalled subverting their desire for food by developing other habits, such as collecting and even hoarding items they did not particularly need, such as books or trinkets. One man wrote: “I’ve been wondering just why I want to buy books so much lately. I’ve always liked to look at books, but now I seem to want to go farther and actually acquire them...I find I’d like to buy clothes, too, some things that I really don’t need. Not being able to buy food

whenever we want to may have something to do with this”.

One man recognized and noted in his diary that he could control his hunger feelings somewhat by diversion activities: “My hunger seems to have some relation to how occupied I may be...I am hungry when I’m not busy at something I am really interested in.”

3.4. Eating Related Behavior During Rehabilitation:

Many men remembered feeling a loss of control over eating during the early re-feeding period. Four men stated that they felt like eating more or less continuously for a long time. Six of nineteen men (32%) reported binge eating (defined as eating large amounts of food in a short period of time along with a feeling of loss of control over eating), particularly during the initial re-feeding period when dietary restrictions were lifted.

Table 1. Eating Changes Resulting from Semi-starvation in 19 Follow-up Participants

• Participants who admitted to binge-eating	<u>N</u>
○ During semi-starvation	0
○ During rehabilitation	6
• Participants who admitted to “overeating” (not binge-eating) during rehabilitation	11
• Participants who vomited (involuntarily) during rehabilitation after “overeating”	2
• Participants hospitalized for gastric distension after “overeating”	1

None of these men reported binge eating before the experiment. One man overate so much that he developed gastric distension and had to be hospitalized. In addition, 11 (55%) reported overeating either because they did not feel satiated with normal meals or

because they continued to eat despite feeling full, and two reported involuntarily vomiting after eating large amounts of food.

When the prevalence of these abnormal eating behaviors was recognized, the Keys

researchers reinstated some control over access to food, except on weekends, when they described a pattern of “weekend gorging”. They estimated that the men initially ate from 50- 200% more food on weekends than during controlled re-feeding. Eight months after the start of rehabilitation, the Keys researchers obtained data on 14 participants and indicated that 10 of the 14 reported eating normal amounts of food and showed less interest in food, although four still thought a lot about food and continued to eat large quantities.

At follow-up, the men did not recall for how long the abnormal eating lasted. Interestingly,

they readily recalled their weights at various times during and after the experiment.

3.5. Weight Changes

We calculated the body mass index (BMI) using the weights and heights of the original participants during all phases of the experiment. During the control period, the mean BMI of the 32 participants who completed the experiment was 21.9 (SD 1.7), and the range was 18.4-25.4. At the end of the semi-starvation period the 32 men remaining in the study had reached the goal of 25% weight loss to a mean BMI of 16.4 (SD 0.9) and a range of 14.9-18.6.

Table 2. BMI of Semi-Starvation Subjects

Phase/Wk	N	Range	Mean	SD
C-12	32	18.4 – 25.4	21.9	1.7
S-24	32	14.9 – 18.6	16.4	0.9
R-12	32	15.6 – 20.7	18.4	1.2
R-33	21	19.6 – 29.2	23.6	2.3
R-58	6	20.0 – 23.0	21.8	1.2

C: Wk of control phase; S: wk of starvation phase; R: wk of rehabilitation; N: number of Subjects; BMI: Body Mass Index (kg/m²); SD: standard deviation

Patients with anorexia nervosa, a disorder characterized by self-imposed restriction of food intake leading to severe weight loss, have a similar BMI range when they enter treatment (9). After 12 weeks of controlled re-feeding, the mean BMI of the Keys participants was 18.4 (SD 1.2; range: 15.6-20.7.), well below their control weights. At that time most men left the formal part of the experiment, except for twelve, who stayed for another 2 months to be monitored on an unrestricted diet. During the first two weeks of unrestricted re-feeding, most participants ate large amounts of food (estimated up to 11,000 calories per day), leading the Keys researchers to re-institute dietary controls.

After a few weeks caloric intake seemed to level off at more reasonable levels of between 3200-4500 calories per day, although some continued to eat much more. Follow-up data were obtained for 21 participants at 8 months of rehabilitation, and for 6 participants at 58 weeks. Table 2 indicates that weights were highest at week 33, with a mean BMI of 23.6 and a range of 19.6 to 29.2. By BMI parameters, five participants were overweight at this time (BMI 25-30), but none were obese (BMI>30).

In the Keys study the participants lost 25% of their control weights during semi-starvation and the mean weight gain exceeding control

weights was 110% at R33. By one year (R 58) weight was obtained for only 8 participants, who had nearly returned to their control weights. The fluctuations in body fat

were more extreme. During semi-starvation, the men dropped to 30% of their control body fat and during rehabilitation body fat rose to approximately 140% (Fig.1).

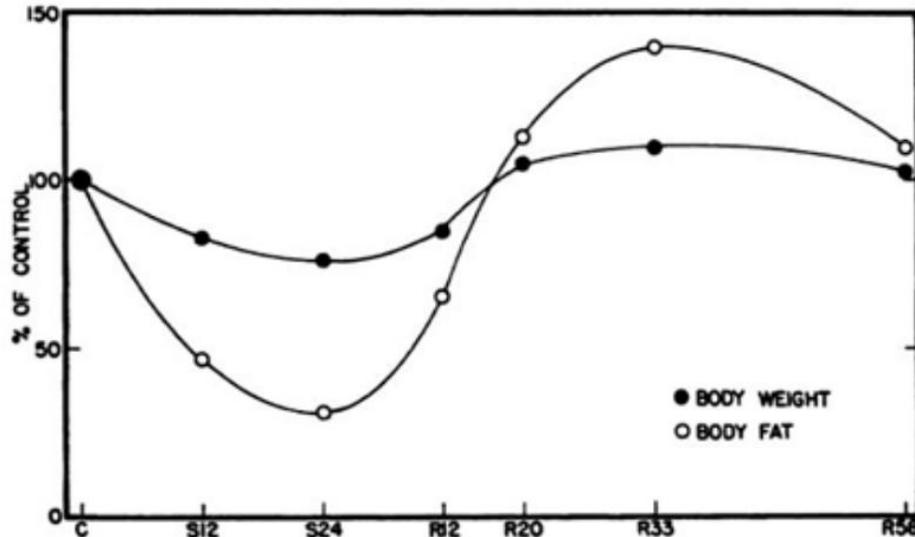


Fig. 1. Body weight and body fat expressed as percentages of control values. C, control; S, weeks of semistarvation, N=32; R, weeks of rehabilitation, N=21 at R33, N=8 at R58.

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By 58 weeks body fat was still somewhat above control values in the 8 participants for whom data were obtained. Based on data gathered in the follow-up, changes in weight were more drastic and lasted longer than reported in the Keys study. The mean weight gain exceeding control weights recalled by 16 follow-up participants was 22 pounds, i.e. 114% instead of 110% of control body weight. Most took longer than 58 weeks to return to their control weight. Seven men had problems for 6 months to a year, 5 had problems for 2 years, one had problems for 3 years, and one had problems that resolved in 4-5 years. Three men described minimal problems with abnormal eating or being overweight. Their weight and eating patterns normalized within 6 months. Three men never returned to their control weight.

The deceased participant who video-taped his experience in 1990 (6) specifically addressed

the fact that he got “fat” after the experiment, weighing from a low of 122 lbs during semi-starvation to 225 lbs about six months later (or 50 lbs above his control weight of 175 lbs). He described feeling hungry and eating almost continuously for a long time. It took him three years to return to his control weight and a normal eating pattern. If his data are included, the average weight gained above control weight in 17 subjects is 27 lbs. or 116 % of control weight.

3.6. Cognitive Changes and Body Perception:

On follow-up, all the men agreed with the original study findings that they experienced some form of intellectual inefficiency during semi-starvation, with either decreased concentration, rate of learning, or poor judgment. Twelve participants on follow-up

recalled decreased motivation and discipline in their intellectual pursuits. Interestingly, on testing during the experiment no objective loss in intellectual ability and no faults in memory or logic were observed (1). Some men carried a full academic load during the experiment.

We inquired about changes in body perception or body image. Two men interviewed said that they perceived others, including study staff, to be overweight during semi-starvation. Two were unaware of their own emaciated appearance although they could see others getting thin. During rehabilitation, seven men were concerned about accumulation of fat in the abdomen and buttocks and five of these men reported that during or after the rehabilitation phase they were bothered by how 'fat' they felt. Three months after the start of rehabilitation one man wrote in his personal notes: "During this week I regained my top standardization (control) weight: however it certainly is not in the same places as the 138 pounds I had on me when I came to Minneapolis. My arms, thighs, buttocks and midsection, all feel fuller than I can ever recall, my face also looks

fatter. However, these reactions may be conditioned by what I got used to during semi-starvation." Six men denied having concerns about changes related to their body.

3.7. Psychological Changes- With Analysis and Review of MMPI Test Results:

The Keys researchers rated all men in good mental health in the control period. During semi-starvation all Keys participants were described as experiencing psychological changes: intense preoccupation with thoughts of food, social introversion, loss of sexual interest, decrease in self-initiated activity, and emotional changes tending toward irritability and depression. While all participants on follow-up confirmed an intense preoccupation with food, a reduction in sexual interest, sociability, and self-initiated activity, only 15 of the 19 men recalled increased irritability and only eight recalled feeling depressed during semi-starvation or rehabilitation.

Remarkably, during rehabilitation the scores indicating recovery from depression correlated with calories received (Fig. 2).

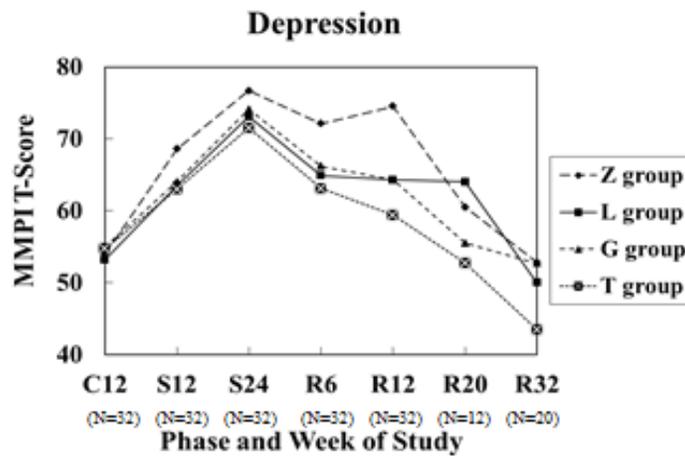


Fig 2. Mean MMPI Depression ratings in Z,L,G,T groups with various calorie diets- Z group with lowest calories, T group with highest calories. C, control period; S, semi-starvation in wks; R, rehabilitation in wks; N, number of participants

During early rehabilitation when diet was tightly controlled (R6 and R12), those who received the least calories (group Z) had high depression scores for the longest time and those who received the most calories (group T) seemed to improve the fastest. During the period of unrestricted food (R20 and R 32), most men remaining in the study ate a high number of calories and all Depression scale scores rapidly returned towards normal.

The Minnesota Multiphasic Personality Inventory (MMPI) was published by Hathaway, a clinical psychologist, and McKinley, a neuropsychiatrist, at the University of Minnesota in 1943 (5); its use in the Keys study was fortuitous. It permitted the Keys researchers to summarize psychological

changes which occurred to varying degrees in all participants under the term “semi-starvation neurosis”, characterized by significantly increased scores on the first three MMPI scales of Hypochondriasis (Hs), Depression (D), and Hysteria (Hy). High scores on the first three scales had become known as the “neurotic triad” after a publication in 1943 on normative data of Minnesota general medical outpatients by McKinley and Hathaway (10).

3.8. The MMPI of 32 Study Completers Which Formed the Basis for the “Semi-starvation Neurosis”

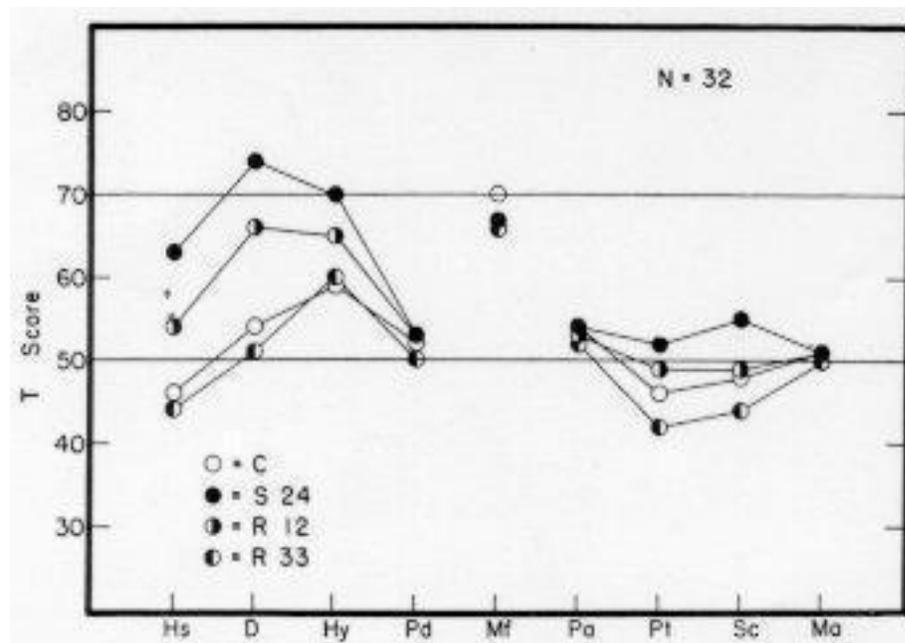


Fig. 3. Mean Scores on the MMPI for 32 semi-starvation participants during the control period (C), after 24 wks of starvation (S24), and after 12 and 33 wks of rehabilitation (R12 and R33). Note: N was only 20 at R33. Hypochondriasis (Hs); Depression (D); Hysteria (Hy); Psychopathic deviate (Pd); Masculinity-femininity (Mf); Paranoia (Pa); Psychasthenia (Pt); Schizophrenia (Sc); Hypomania (Ma).

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Fig. 3 displays MMPI scores for the 32 semi-starvation participants who completed the experiment. All scales were uncorrected for K, a later test development that corrected empirically for psychological defensiveness, and had a mean score of 50 with a standard deviation of 10 in the normative population. The highest mean score during semi-starvation was Depression (more than 2 SD above normal), followed by Hysteria at 70. This profile type suggests a depressive reaction with anxiety in a hysteroid personality (11). The Depression score and MMPI profiles of 20 participants obtained after 33 weeks of rehabilitation returned to the “normal” pre-semi-starvation level. Of note is that the Psychopathic deviate (Pd) scale and the MMPI scales indicating “psychotic” tendencies (Pa (paranoia), Pt (psychasthenia), Sc (schizophrenia), and Ma (hypomania) remained within normal limits during all phases of the experiment in the participants who completed the experiment. The normal Pd score indicates a lack of impulsivity, aggressiveness, rebelliousness and a general lack of anti-social features, not unexpected in conscientious objectors with religious affiliations. In essence, these men were normal as a group before the experiment, the psychological changes during semi-starvation were measurable on the MMPI and formed the basis for inferring a “semi-starvation neurosis”, and they returned to normal values after the imposed stress. Validity scales L, F, K in the MMPI descriptions or profiles were not included, and no K correction was made for the 5 scales (Hs, Pd, Pt, Sc, and Ma), which could affect interpretation of the MMPI’s for non-volunteer samples.

According to Schiele and Brozek (8), 5 of the 32 study completers developed symptoms that went beyond the range of “semi-starvation neurosis”. They developed serious clinical worsening during the starvation phase, which was reflected in changes in their MMPI. We were able to interview 2 of these participants: One participant who had a mild

cyclothymic history prior to the experiment, experienced several episodes during the initial part of the starvation phase lasting no more than a few days of exaggerated mood changes consisting of elation followed by “deep, dark depression”. During the last 3-4 weeks of the starvation phase he suffered a severe depression and he thought he was going “crazy”, although he was able to continue with the experiment. The MMPI indicated a high depression score and an increase in the Pt and Sc scales consistent with his psychological decompensation (such a profile is consistent with that of patients diagnosed as schizophreniform psychosis). The severe depression gradually resolved during the rehabilitation phase (8). At follow-up, he denied having any further psychiatric problems and went on to have a varied and successful national and international academic career.

Another participant had a history of being a hard worker, driving himself hard to finish a task, but then being “compelled to go to bed at home for an extended period of recuperation” (8). He experienced a severe depression and psychological decompensation at the end of the starvation period that culminated in two attempts at “unconscious” versus accidental self-mutilation by chopping off three fingers of his left hand while chopping wood. He recovered quickly after a brief hospitalization and was able to complete the experiment. At follow-up, this man described a successful life, but reported a low-grade chronic depression for 4-5 years prior to the interview related to stressful life experiences.

3.9. The MMPI of Four Non-Completers.

The MMPI scores of the 4 men who failed to complete the experiment due to their significant dietary violations and failure to lose sufficient amounts of weight were also normal during the control period. They showed the typical “semi-starvation neurosis” increases in the Hypochondriasis, Depression

and Hysteria scales during the starvation phase, yet 3/4 showed a significant increase on the Pd scale during starvation, indicating increased anger, impulsivity, aggressiveness or passive-aggressiveness, rebelliousness, or other anti-social features. There were also marked elevations of the “psychotic” side of

the MMPI profile, although not reaching abnormal values. Longitudinal MMPI profiles for one of these participants under the experimental conditions are shown in Fig. 4. K-correction would have led to a psychotic-like profile (Fig.4).

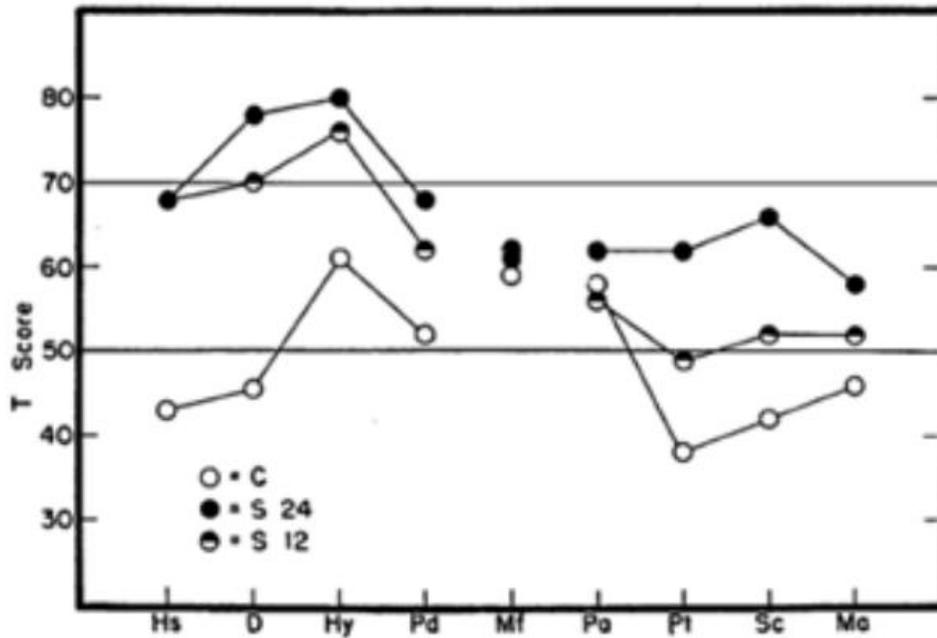


Fig. 4. Scores on the MMPI participant No. 232 during the control period (C), and after 12 and 24 weeks of starvation (S12 and S24). Hypochondriasis (Hs); Depression (D); Hysteria (Hy); Psychopathic deviate (Pd); Masculinity-femininity (Mf); Paranoia (Pa); Psychasthenia (Pt); Schizophrenia (Sc); Hypomania (Ma). From Keys et al. (1950)(1). Copyright 1950 by the University of MN Press.

Two of the four men who failed to complete the experiment due to dietary violations had to be hospitalized psychiatrically because of severe decompensation and “pre-psychotic” symptoms. During the first few weeks of

semi-starvation one of the men began to have strange dreams of “eating senile and insane people”. His MMPI profile suggests similarity to patients diagnosed with a schizoaffective psychosis (Fig 5).

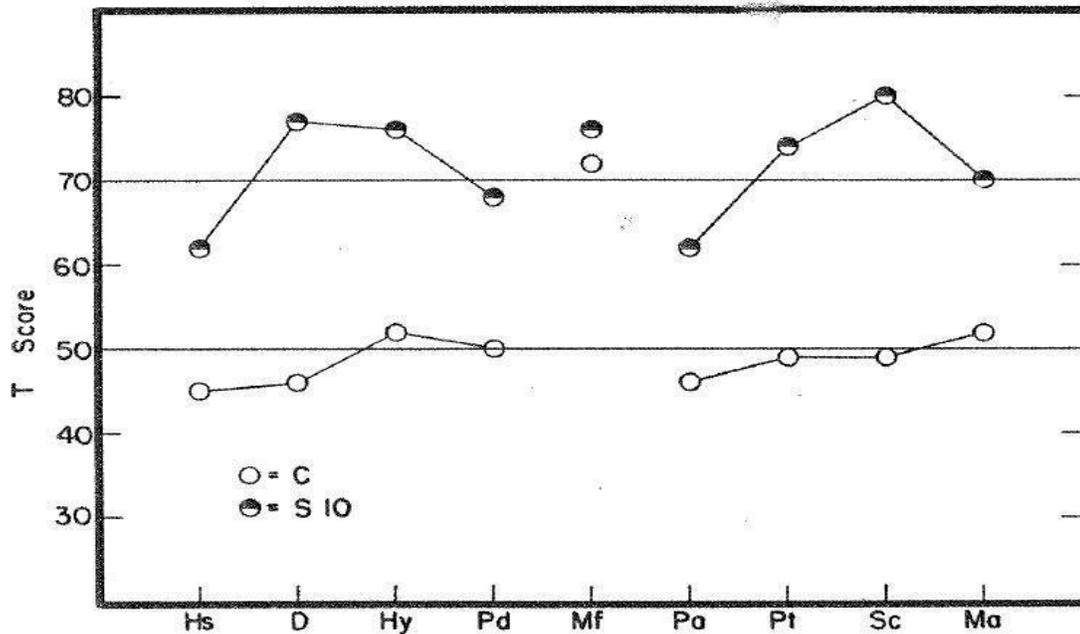


Fig. 5. Scores on the MMPI for participant No. 234 during the control period (C), and after 10 weeks of semi-starvation (S10). Hypochondriasis (Hs); Depression (D); Hysteria (Hy); Psychopathic deviate (Pd); Masculinity-femininity (Mf); Paranoia (Pa); Psychasthenia (Pt); Schizophrenia (Sc); Hypomania (Ma). From Keys et al. (1950)(1). Copyright 1950 by the University of MN Press.

He then began impulsively to break the controlled diet, concealed his dietary violations and began minor shoplifting sprees stealing candy and trinkets that had no value for him. He wrote voluminously and showed a distinct flight of ideas. He then developed a violent emotional outburst threatening suicide and violence; he was admitted to a psychiatric ward. The clinical picture suggested hypomania: he was overly talkative, elated and emotionally labile. He quickly returned to normal after being allowed to eat ad libitum. We learned that this man died sometime after the original experiment. We were unable to get any follow-up information for him.

The other man began to use enormous amounts of chewing gum (40-60 packs per day) and later stole some food items. He began to compulsively root in garbage cans

and actually ate garbage. Since he failed to lose weight despite drastic cuts in his diet, he was dropped from the experiment at the end of the starvation period. Subsequently he ate huge amounts of food, became sick and vomited. He sought psychological help and voluntarily sought admission to the psychiatric ward twice in a short period of time. "His symptoms subsided over a period of weeks and he eventually made a satisfactory adjustment" (8). We interviewed this participant at follow-up. He told us he gained about 30 pounds above his control weight after the starvation period by overeating and was bothered by looking fat. It took him about a year to return to normal eating and normal weight. He denied any further psychiatric problems and eventually earned a PhD.

4. Comparison to Eating Disorders

4.1. Importance of Temperament and Personality—Relationship to Nutritional Status, Psychological State and Abnormal Eating Pattern.

Personality and temperamental differences have been described between the restricting and bulimic subtypes of anorexia nervosa (12, 13). Those who lose weight by persistently curtailing their food intake tend to be more introverted and conscientious, more parsimonious, better organized; in short they display higher emotional self-control and self-discipline, whereas those who develop binge-eating and then vomit to lose weight tend to be more outgoing, sometimes more impulsive, and tend to be less controlled behaviorally and emotionally

The rise in the scores on the “neurotic” scales of the MMPI’s with prolonged semi-starvation in the 32 men who completed the experiment is similar to the elevation in the “neurotic triad” observed in eating disorders (14). In general, restricting anorexia nervosa patients show less psychopathology on the MMPI than patients who binge eat (14-16). In restricting anorexia nervosa the depression scale is generally the highest; no published study has shown a mean profile exceeding 70 on a clinical scale (16). Notably, Vitousek and Manke (16) have pointed out that the mean semi-starvation profile for the 32 participants who completed the experiment in the Keys study looks remarkably similar to the average profile for restricting anorexia nervosa. Like the MMPIs in the Keys study participants, once they regained pre-starvation weights, the MMPI of low weight anorexia nervosa patients (with and without binge eating) becomes more normal with weight gain in a hospital setting (17, 18), indicating that the MMPI cannot be interpreted without taking the clinical context into account.

Patients who binge eat (both bulimic anorexia nervosa patients and normal weight bulimia nervosa patients) consistently show higher Pd

scores and sometimes higher scores in the “psychotic” end of the MMPI (particularly the Paranoid (Pa), Psychasthenia (Pt), and Schizophrenia (Sc) scores), a profile frequently associated with impulse and characterological problems (14-16, 19). Interestingly, the MMPI profile of female bulimia nervosa patients (14) is similar to that of the male semi-starvation subjects who failed to complete the experiment due to dietary violations who showed marked psychological worsening and developed binge eating and kleptomania (Fig.4 and 5). The main difference is a peak in the Hy scale in the semi-starvation subjects not seen in the bulimia nervosa patients.

4.2. Hunger, Preoccupation with Food and Eating Patterns:

Keys and Brozek (1) erroneously assumed "a decreased appetite" in anorexia nervosa and believed that “continuous hunger and mental absorption with food” were absent in anorexia nervosa. In fact, the behaviors described in the experimental participants, such as collecting recipes and cookbooks, and hoarding food and “strange” items, and even kleptomania, are characteristic of anorexia nervosa. Anorexia nervosa patients are preoccupied with and dream about food, reflecting hunger sensations, even if they may deny being hungry (2, 20). When asked about appetite in one study evaluating 44 hospitalized pre-treatment anorexia nervosa patients, 54.5% claimed to have no appetite, and 45.5% admitted to a strong appetite, but were afraid of losing control of their appetite (21).

Keys and Brozek (1) were also unaware that abnormal eating patterns such as binge eating can occur in anorexia nervosa, as observed by Halmi et al (21). In a systematic study by Casper et al. (12), the clinical importance of bulimic behavior in anorexia nervosa was analyzed leading to its recognition as a distinct diagnostic subcategory (DSM IV). Food restriction, due to dieting, often with significant weight loss is a recognized

antecedent to most cases of binge eating and bulimia nervosa (22, 23).

4.3. Energy Levels and Physical Activity Patterns in the Minnesota Semi-Starvation Study and Anorexia Nervosa.

All signs of physiological starvation described in the Keys study, with the exception of the markedly diminished energy levels and physical activity patterns, have also been described in anorexia nervosa (2-4).

As weight loss progressed, the Keys researchers noted and the follow-up participants vividly recalled the marked loss of energy, increasing lethargy and weakness. None of the follow-up participants recalled periods of physical activation, even though the Keys researchers noted in some short-lived "quickening", usually associated with transient euphoric feelings lasting from a few hours to several days followed by a "low" period.

This lethargy is in sharp contrast to the mostly normal, if restless, energy levels and normal or higher than normal activity levels in anorexia nervosa (24, 25). Bruch (26) noted that "the subjective feeling of not being tired and ...the drive for activity continues until the emaciation is far advanced". In the Keys study the men's alertness decreased, unlike the "paradoxical liveliness" in anorexia nervosa already described by Lasègue (27). It is interesting that the Keys researchers recognized that this 'drive for physical activity' seems to be a fundamental clinical and psychopathological feature for differentiating anorexia nervosa from the lethargy and slow movements observed in other conditions of human starvation (1). Several studies have experimentally confirmed normal or higher activity levels in severely underweight and fasting anorexia nervosa patients (28, 29). Physiologically these activity levels appear to be starvation-dependent (30). As a result, unlike the men in the Keys study who dreaded exercise, anorexia nervosa patients like to exercise, behavior with the added benefit of reducing stress while

accelerating the desired weight loss (25, 31-33).

4.4. Body Perception Changes

Two men interviewed said that they perceived others, including study staff, to be overweight during semi-starvation while two were unaware of their own emaciated appearance. During the rehabilitation phase seven men were concerned about accumulation of fat in the abdomen and buttocks and five of these men reported they were bothered by how 'fat' they felt. Nonetheless, these realistic concerns about fat accumulation during weight gain are different from the body image changes in anorexia nervosa patients, who sometimes describe themselves as "fat" despite being extremely thin (34). In anorexia nervosa patients, the tendency for increased fat accumulation in the abdominal area during rapid therapeutic hospital nutritional rehabilitation is common (35).

DISCUSSION

The Minnesota Experiment on the Biology of Human Starvation (1) measured and documented for the first time that prolonged caloric under-nutrition resulting in significant loss of body weight in normal men led to down regulation of physiological functions and changes in psychological function, all reversible with qualitatively and quantitatively adequate food intake. Our follow-up evaluation provides new data suggesting that the severe food restriction resulted in abnormal eating patterns and weight changes that were more prolonged than reported by Keys et al (1), given that the original follow was no longer than 8 months.

Furthermore, our long-term follow-up study suggests that voluntary severe food restriction for 6 months was not associated with life-long physical, cognitive or emotional adverse effects, despite significant individual suffering during the experiment. All but one man stated

they would again participate in the experiment. All participants ultimately led interesting and productive lives, perhaps not unexpected in view of their voluntary participation as conscientious objectors and the original selection criteria for physically and psychologically healthy subjects.

Previous publications have noted the relevance of the Minnesota experiment to anorexia nervosa, emphasizing the similarity to signs of starvation in anorexia nervosa (2-4, 36) and therapeutic benefits from recognizing signs of starvation in anorexia nervosa (3,4). The study by Kalm and Semba (37) is particularly relevant because it involved tape-recorded follow-up interviews of 18 Keys study participants in 2003-2004, thus following and overlapping with our 19 participant follow-up in 2002. Their detailed description of the Minnesota experiments provides a lively account interspersed with the men's recollections of the semi-starvation and rehabilitation experiences. While their general findings converge with our findings, our study focuses more specifically on changes in eating, weight, psychological state, and the relevance to eating disorders.

Keys and Brozek (1) recognized from the men's reactions during rehabilitation that prolonged semi-starvation can result in overeating and binge eating and hence introduced controlled meals. Similar eating patterns have been observed under conditions of enforced starvation. Polivy *et al* (38) compared Canadian WWII combat veterans who were interned in German prisoners of war (POW) camps with non-POW veterans. The POW group reported significantly more binge eating than the non-POW group; the greater the weight loss the more binge eating years later. Favaro *et al* (39) observed that former political prisoners with severe weight loss who survived Nazi concentration camps were at greater risk of developing recurrent binge eating than the ex-partisans with less weight loss. Binge eating often, but not always, started immediately after liberation and then persisted for many years, in

some for 51 years. In Holocaust survivors, Sindler *et al.* (40) described intense preoccupation with and sensitivity to food-related issues. By contrast, a retrospective study of Holocaust survivors in Israel did not find that prolonged and severe starvation resulted in the experience of binge eating compared to a control group of immigrants, matched for schooling and origin (41). The sufferings of the malnourished concentration camp survivors and the dangers of eating in excess are movingly described in a paper by Brooks (42).

Observations from the Keys study suggest that food restriction does not lead to binge eating in everyone. Personality and temperament seems to play a part in the type of response. One follow-up participant, Max Kampelman, who described himself as having "considerable ability to focus on goals and being a bit stubborn", was able to "concentrate when others couldn't study". He finished law school during the starvation phase and had the least psychological worsening on interview and on the MMPI (1,8). During rehabilitation he never felt a loss of control over eating, never binge ate, and had returned to normal eating and his former weight within six months. Several other men denied binge eating and described returning to normal eating and weight quickly. In contrast, the 4 participants who failed to complete the experiment due to their significant dietary violations and developed binge eating and kleptomania, showed marked psychological worsening during semi-starvation. The Keys researchers recognized that the emergence of individual differences in basic personality make-up was associated with the response to semi-starvation. They remarked that "Ex post facto" it appeared that men with a more stable personality makeup showed minimal deterioration while those with latent personality weaknesses developed more severe symptoms" (8).

The Keys study authors found underlying personality characteristics to be a factor in the severity of MMPI changes with long-term

caloric under-nutrition. These observations apply to eating disorders. The MMPI profiles of Keys study participants who had difficulty adhering to the requirements of semi-starvation resemble those of patients with bulimia nervosa (14), while the mean semi-starvation profile of the 32 subjects who completed the Keys experiment looks remarkably similar to the average profile for restricting anorexia nervosa patients (16). Also, like the return to more normal MMPI's associated with weight regain in the Keys study, the MMPIs of low weight anorexia nervosa patients, with and without binge eating, become more normal with weight gain (17, 18). Thus, the Keys study supports the fact that a return to a normal nutritional state is required for eating disorder patients to improve psychologically.

Psychologically, the lethargy and emerging depressive symptoms in the Keys study participants stand in contrast to the mental alertness and continued vigor expressed by anorexia nervosa patients. Physically, loss of energy, fatigue and muscle weakness experienced by participants in the Keys study are not observed until the cachectic end stage of anorexia nervosa. For most of the disorder, anorexia nervosa patients preserve their energy, remaining active and mobile and not infrequently show greater than normal activity levels (2, 24, 30).

Another difference from anorexia nervosa was the absence of pathological body perception disturbances and disparagement in the Keys study participants. Some men expressed reasonable concern and critical evaluation of their changing body shape during nutritional rehabilitation. In anorexia nervosa, the critical evaluation of their changing body tends to intensify the fear of weight gain.

Gender differences may play a part in the response to semi-starvation. The Keys subjects were all male, whereas eating disorders occur predominantly in females. This sex difference might contribute to the symptoms in anorexia nervosa, such as the body perception

disturbance. It might be involved in the continued normal or high activity levels, since severely food-restricted female compared to male rats show higher running wheel activity (43).

This follow-up study could have been improved utilizing a more highly structured interview format. One might also question whether a sample of 20 of 36 original participants is truly representative. There is, however, no reason to believe that 19 men who were interviewed plus the deceased participant who had made a videotaped interview were different from the 10 other men who had died or the 6 men who could not be located. Furthermore, the accuracy of information based on retrospective recall when tested against the facts has limitations. For example, only 8/19 men we interviewed recalled feeling depressed, although the Keys study reported that all men had some measurable depressive symptoms. Remarkably, all men spontaneously remembered severe lethargy with weight loss and a lack of motivation and surprisingly, nearly all recalled periods of abnormal eating and their maximum weights as well as the period of time it took to return to their pre-experiment body weights.

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