BIOGENA STUDY

The influence of Biogena fit@work® Stressbiotic on irritable bowel syndrome, stress intensity and recovery

Results of a six-week intervention study on stress-induced intestinal disorders

Summary

Irritable bowel syndrome (IBS) has a high prevalence. Roughly twelve million people in Germany suffer from functional bowel disorders. Individual stress levels play an important role in this context. Stress can affect gastrointestinal functions by activating the stress axis (HPA axis), altering the microbiome, and triggering irritable bowel syndrome.

The symptoms of irritable bowel syndrome then aggravate the patient's physical and psychological stress levels. IBS is stress sensitive; chronic stress is believed to be relevant for prognosis.

The following observational study demonstrates that the use of natural substances can have a beneficial effect at various levels of this complex phenomenon.

Biogena fit@work® Stressbiotic, a combination preparation containing probiotic bacteria, saffron extract and various key vitamins, can reduce the intensity of IBS symptoms, lower stress levels, improve recovery after work-related stress situations and ultimately improve patients' satisfaction with life.

Background:

There is a strong link between irritable bowel syndrome and stress. The intestine and nervous system use a number of different pathways to communicate with each other. The two organs are connected via the neuronal signaling pathways of the autonomic and sympathetic nervous systems, and they are also closely linked via the stress axis (hypothalamic-pituitary-adrenal axis or HPA) (Fig. 1) and the immune system. [1] Stress, stress reactions and the release of stress hormones thus have a significant impact on the functions of the gastrointestinal tract. For example, stress can disrupt digestion and the intestinal flora, and can even trigger functional bowel disorders, irritable bowel syndrome and intestinal diseases.[2]

High prevalence of IBS – especially among women

Approximately 50 per cent of adult patients suffering from chronic abdominal pain and irregular bowel movements have functional bowel disorders. This means that routine diagnostics are unable to provide conclusive results that adequately explain their symptoms.[3] Physicians generally diagnose irritable bowel syndrome by excluding all other possible causes.

Approximately 10–20% of the world's population is affected by IBS, women roughly twice as much as men.[2] Health insurance providers have estimated that there are approximately twelve million IBS sufferers in Germany alone.[4] Irritable bowel syndrome and functional bowel disorders have far-reaching consequences for patients' everyday lives. They are associated with impairments of varying degrees, affecting both professional and private life, and have been shown to greatly reduce individuals' quality of life.

Stress alters the microbiome – the microbiome influences our perception of stress

There is a strong link between IBS and physiological stress reactions. Stress affects gastrointestinal health at a number of levels. Stress-induced changes to the microbiome are an important factor here. Chronic stress has been shown to reduce bacterial biodiversity in the intestinal tract. In addition, stress situations tend to favor the proliferation of pathogenic bacterial species at the expense of the beneficial lactobacteria.[2] Conversely, there is evidence that dysbiosis, i.e. this shift in the microbiome in favor of pathogenic germs, can have a negative effect on the patient's mental state and mood.

Stress also contributes to making the natural barrier of the intestinal mucosa more permeable to pathogenic bacteria. This activates the immune system, which in turn affects the composition of the bacterial flora and activates the stress axis (HPA axis). Facultative pathogenic intestinal microbes such as Escherichia coli thus play a crucial role in the body's stress response.[5]

In addition to increasing the permeability of the intestinal mucosa, stress changes the body's digestive performance, and intestinal motility and perfusion. This can trigger an intensive activation of mast cells, which in turn increases the release of proinflammatory cytokines and stimulates the stress axis (Fig. 2). [2]

Basic measures – lowering stress levels

Normalizing stress responses in patients with functional bowel disorders and IBS could prove to be the basis for therapeutic success. One way of achieving this is to introduce measures that regulate the stress axis (HPA axis). Another key factor is the stabilization or re-establishment of beneficial flora in the intestines by probiotic microorganisms.

Selected strains of bacteria, plant extracts and vitamins, whose effect profile has been scientifically documented, offer the possibility of modulating the body's stress response patterns at both levels, i.e. along the HPA axis and in the microbiome. The combination preparation Biogena fit@work® Stressbiotic was developed for this therapeutic approach.
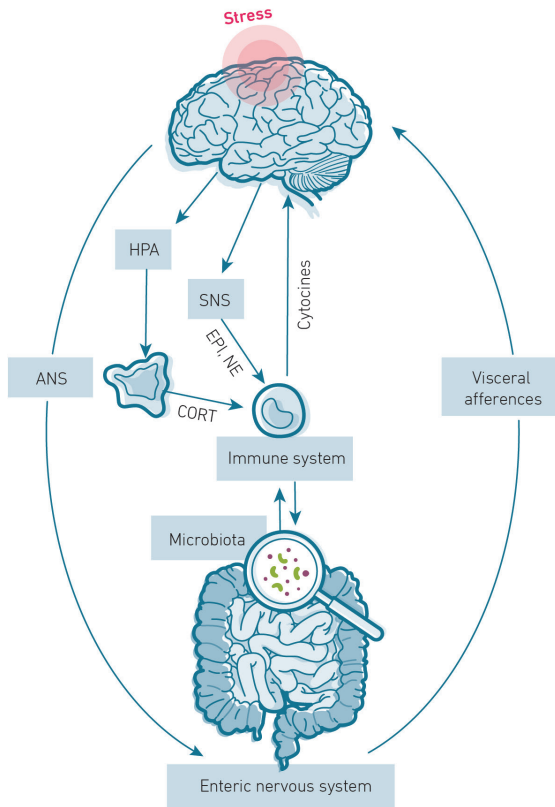
Fig. 1: Signaling pathways of the gut–brain axis: Schematic representation of the bidirectional axis and its principal afferent and efferent connections that can be activated or modulated by stress. (ANS: autonomic nervous system; SNS: sympathetic nervous system, HPA: hypothalamic-pituitary-adrenal axis; EPI: epinephrine; NE: norepinephrine; CORT: cortisol), adapted from Labanski et al., 2020[11]
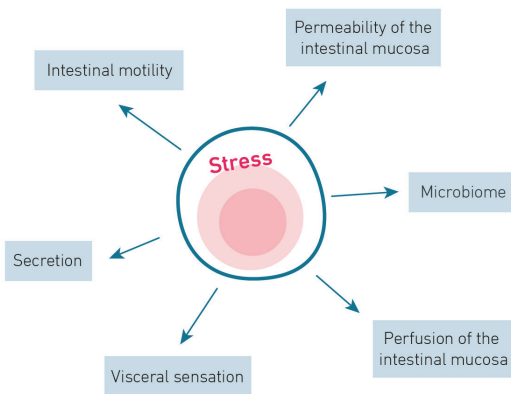

Fig. 2: The effects of stress on gastrointestinal functions[2]

The study

The aim of this observational study was to verify that the combination preparation Biogena fit@work® Stressbiotic has a beneficial effect on the intensity of gastrointestinal symptoms experienced by IBS patients, their individual stress levels, and their ability to recover.

The product:

Biogena fit@work® Stressbiotic is a combination preparation containing selected bacteria cultures (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175), saffron extract and vitamins B$_2$ and C.

A clinical study has already demonstrated that the combination of bacteria used in the treatment can significantly improve stress-related anxiety and sleep disorders.[6] The beneficial effect of saffron on depression has been demonstrated in a meta-analysis.[7]

Vitamin B is essential for maintaining the integrity of the intestinal mucosa, and the antioxidant vitamin C plays an important role in both mental and immune system functions. This data forms the basis for the assumption that the product should be effective in relieving the symptoms of stress-induced IBS.

The method:

In May 2020, 101 people who suffered from various stress-induced intestinal and digestive disorders were recruited via social media. 93 participants completed the study properly, and their data was admitted for analysis. 86 % of them were women and 14% men. They were recruited from Austria, Germany, Switzerland, Italy and Spain. The women's average age was 38 years, the men's was 37.

The intervention period was six weeks, during which one capsule of Biogena fit@work® Stressbiotic was taken daily.

IBM SPSS Statistics 25 was used to calculate the statistics.

The results

Highly significant improvement of IBS symptoms: up to 30 %

An IBS diagnosis is made on the basis of gastrointestinal disorders such as abdominal pain, abdominal cramps, flatulence, irregular bowel movements, diarrhea or constipation with no pathological findings. Functional bowel disorders are defined by the above-mentioned set of symptoms, a period of at least three months, and the exclusion of any other diseases that might adequately explain the symptoms.[3] Participation in the observational study was conditional on the presence of prolonged or chronic intestinal and digestive disorders.

At the beginning of the study, 91 % of the participants (85 individuals) stated that they had been suffering from the above symptoms for more than six months. 26 participants (28 %) even reported experiencing chronic intestinal disorders. 16 participants (17 %) were under medical treatment for intestinal disorders. 51 participants (55 %) also suffered from food allergies or intolerances.

The type and intensity of the symptoms were assessed using SoP (Severity of Problem) scores. Various issues affecting the gastrointestinal tract were grouped into five categories: general digestive disorders, pain, changes in appetite, social problems caused by irritable bowel syndrome, and use of medication (Table 1). Participants were asked to rate the intensity of their symptoms on a numerical scale from 0 to 10, from 0=never/not at all to 10=always/intolerable.

Digestive disorders	• Constipation • Diarrhea • Alternating constipation & diarrhea • Irregular bowel movements
Pain, cramps, flatulence	• Abdominal pain, abdominal cramping • Flatulence
Changes in appetite	• Hunger flashes • Loss of appetite
Social problems	• Impaired professional & family life • Impaired social life
Use of medication	

Table 1: Breakdown of SoP categories with regard to individual irritable bowel symptoms

The baseline assessment reveals a high discomfort score, with an average of 7.1 points in the category *pain, cramps,* and *flatulence,* followed by the categories *digestive disorders* and *social problems,* each of which scored a medium discomfort score of 4.9 points (Fig. 3).

In pain diagnostics, a score of 4 points or more is generally accepted as the trigger threshold for initiating therapy.

The evaluation of the data shows that, on average, all SoP scores improved highly significantly after the six-week intervention, with the exception of the point regarding the *use of medication* to relieve intestinal disorders. There was a 19% reduction in the intensity of the symptoms in the category *pain, cramps, flatulence;* intensity was reduced by 18 % in the category *digestive disorders,* by 13 % in *changes in appetite,* and by as much as 30 % in *digestion-related social problems* (Fig. 4).
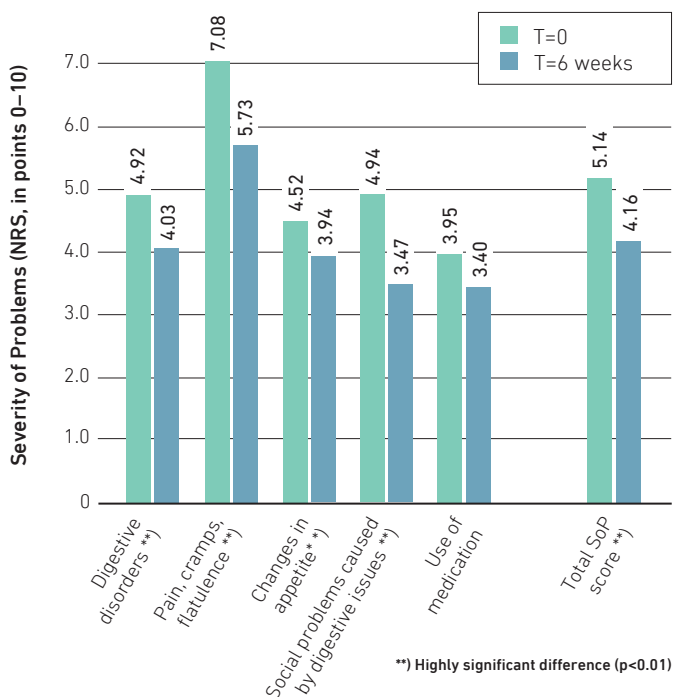

Fig. 3: Individual assessment of the severity of the symptoms (SoP scores) using NRS (0 to 10) at the beginning and after 6 weeks of taking 1 capsule of Biogena fit@work® Stressbiotic per day (n=93)

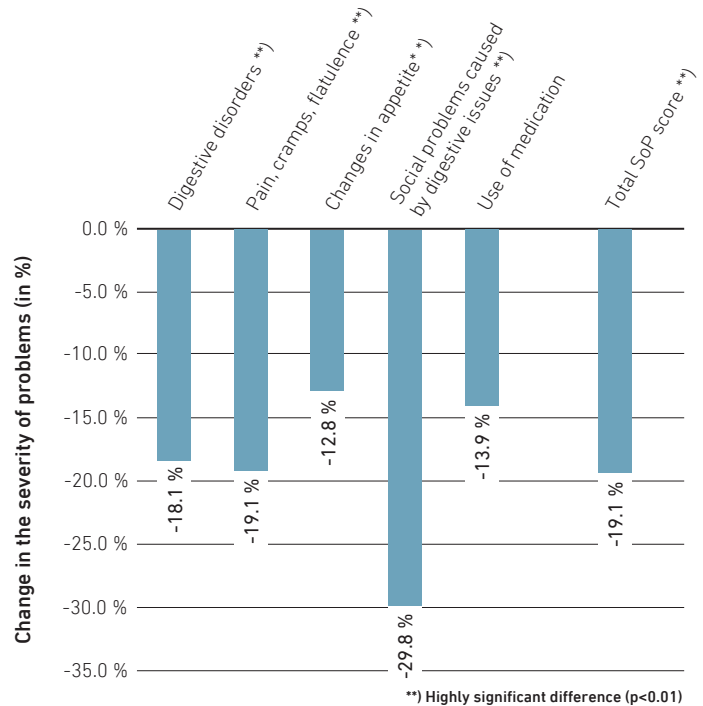**) Highly significant difference (p<0.01)

Fig. 4: Decrease in intensity of symptoms in SoP categories in % after taking 1 capsule of Biogena fit@work® Stressbiotic per day for 6 weeks

Depending on their intensity, functional bowel disorders can lead to severe physical and social impairment. Besides classical digestive issues such as constipation and diarrhea, patients report that pain, cramps and flatulence have a detrimental effect on their professional, social and family lives.

There is some discussion of a possible connection between IBS symptoms and social avoidance behavior patterns up to and including social phobias. For example, there is some evidence indicating that anxiety disorders and depression are more common in children with functional abdominal pain as compared to healthy children.[8] The reduction of IBS related social restrictions by an average of 30 % is an important indicator of the relevance of the product in patients' ability to cope with day-to-day life.

Stress levels are reduced by a third

Stress occurs when individual resources are not sufficient to meet external requirements. Stress triggers physiological reactions that can cause various health problems if they persist or recur. The gastrointestinal system is particularly susceptible: stress can have a significant impact on the functions of the digestive tract via the neuronal networks (brain-gut axis) and endocrinal and immunological stress mediators.[9]

Acute stressors alter the body's neuronal, endocrinal and immunological responses via the HPA axis. These responses are associated with the development and onset of IBS. Irritable bowel syndrome is therefore also termed a stress sensitive disorder.[10]

Studies show that IBS patients suffer from higher work-related stress than healthy individuals, which is reflected in a higher release of pro-inflammatory cytokines.[11] Chronic stress is also believed to be a relevant factor for prognosis. For example, patients who suffered from constant stress experienced no

improvement in their intestinal symptoms over six months compared to 44 % of patients whose stress levels were low. [8]

Elevated stress levels were a significant factor for the participants of this study as well. Individual stress levels were assessed using the internationally recognized DASS questionnaire (Depression Anxiety Stress Scale). Stress intensity is calculated on the basis of seven individual items. A score of over 14 is associated with elevated stress levels.

At the beginning of the observational study, the participants scored an average of 24.8 points, putting them near the upper threshold of the moderate stress category (19–25 points), just below the cut-off point for severe stress (26–33 points). After using Biogena fit@work® Stressbiotic for six weeks, participants scored an average of 16.8 points, placing them within the moderate stress range, close to the threshold for normal stress levels (0–14 points) (Fig. 5). The total stress score showed a highly significant reduction of 8 points (32 %).

Highly significant improvements were achieved in the total DASS stress score and in all the DASS stress items (Fig. 6), which suggests that the intervention had a fundamental effect on participants' stress levels.

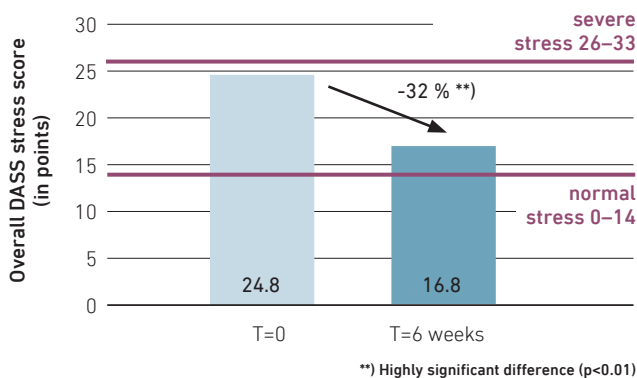**) The reduction of all stress scores is highly significant

Fig. 6: Changes in individual stress items and total stress score (according to DASS, in %) after 6-week intervention with 1 capsule Biogena fit@work® Stressbiotic per day (n=93).

**) Highly significant difference (p<0.01)

Fig. 5: Stress intensity (according to the DASS scale) at the beginning and end of the intervention involving 1 capsule Biogena fit@work® Stressbiotic per day for 6 weeks (n=93). The decrease is highly significant at 32 %.

Improved ability to recover after work-related stress

For most people, work is one of the principal sources of stress. In this context, the ability to recover after work is an important factor in managing stress-related physical and psychological problems. High levels of stress at work can impair mental recovery processes during non-working hours and may lead to an accumulation of negative stress symptoms,[13] which are ultimately also linked to IBS.

Conversely, studies also show that the ability to mentally switch off from work correlates positively with workers' well-being and their physical and mental health.[13] The so-called recovery paradox refers to the phenomenon where higher stress levels limit our ability to recover, thereby promoting negative health effects.[14]

The Recovery Experience Questionnaire (RECQ) was used to measure the participants' ability to recover after stress events.

Recovery is the process that restores mental and physical functions to their original level, before the stress event.[12]

Measuring patients' ability to recover during non-working hours is therefore an additional option for demonstrating the changes that an intervention can bring about in stress-related functional bowel disorders. The recovery experience is quantified by means of the Recovery Experience Questionnaire (RECQ) using four items. The results can be compared over time. This makes the questionnaire suitable for monitoring the course of stress-related IBS symptoms.

The RECQ comprises four dimensions: psychological detachment from work, the ability to relax, mastery (seeking mental and physical challenges) and control over personal leisure activities.

In the Biogena fit@work® Stressbiotic intervention study, the results of the RECQ matched the positive results obtained for intestinal disorders and stress. On average, the study participants showed improvements in all four dimensions, with the most significant increase in the items relaxation at +7.9 % and psychological detachment from work at +6.3 %. In both cases, the differences between the results at the start and end of the intervention were significant or highly significant (Fig. 7).

*) Significant difference (p<0,05)
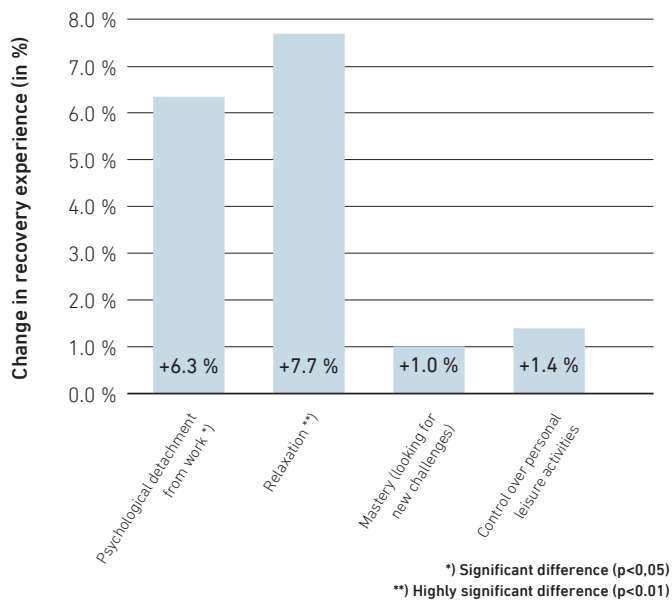**) Highly significant difference (p<0.01)

Fig. 7: Percentage changes in the four dimensions of the Recovery Experience Questionnaire (RECQ) after a 6-week intervention with 1 capsule Biogena fit@work® Stressbiotic per day (n=93)

*) Distribution between T=0 and T=6 weeks shows significant differences (p=0.039) McNemar test
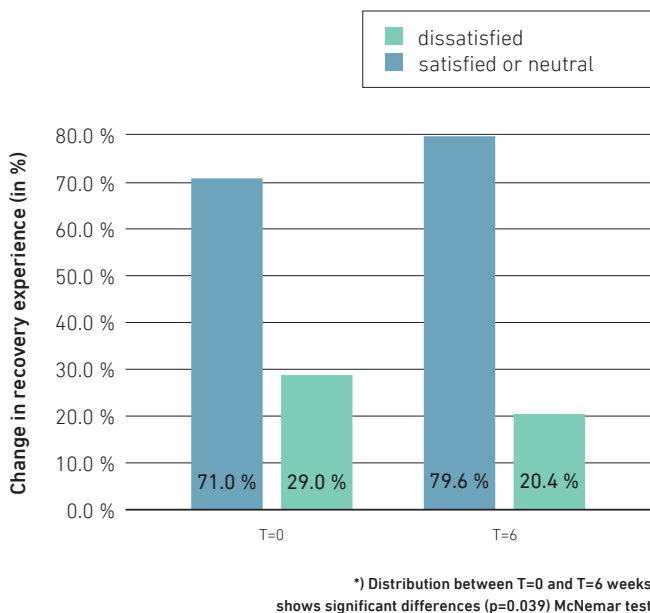
Fig. 8: Percentage of participants who were satisfied with their life (SwL score ≥ 20) or dissatisfied (SwL score < 20) at the beginning and end of the intervention involving 1 capsule Biogena fit@work® Stressbiotic per day for 6 weeks (n=93)

Life satisfaction as an indicator of relevance

In addition to statistical significance, which assesses the scientific robustness of the results obtained, the relevance of the measured changes for the individual is also an important consideration. Relevance, i.e. the sum of individually perceived improvements, can be determined by measuring quality of life and life satisfaction. In this study, the participants' life satisfaction was measured at the beginning and end of the intervention using the internationally accepted SwL (Satisfaction with Life) scale.

The SwL scale is used to evaluate life satisfaction on the basis of five items. The possible range of scores is 5–35. Scores below 20 indicate that the respondent is dissatisfied with life, whereas scores above 20 indicate satisfaction with life.

Intervention with Biogena fit@work® Stressbiotic led to a statistically significant increase in the participants' average overall life satisfaction score (SwL scale). The number of participants who were satisfied with their lives also increased significantly. Conversely, the number of dissatisfied respondents decreased by 30 % (Fig. 8).

Conclusion:

Stress can trigger IBS, and IBS causes more stress. In order to interrupt this self-perpetuating cycle of cause and effect, interventions on several physiological levels can be useful. In this context, it is just as important to create and stabilize a health-promoting microbiome as it is to normalize the activity of the stress axis (HPA axis). It is reasonable to assume that the simultaneous treatment of both systems will intensify the effects, thus leading to a faster and more powerful reduction of IBS symptoms and ensuring lasting therapeutic success.

In this observational study, this approach was tested in practice using the combination preparation Biogena fit@work® Stressbiotic. The results confirm the initial hypothesis that the product can significantly reduce IBS symptoms and stress. At the same time, it can improve patients' ability to recover during non-work hours, which in turn leads to greater life satisfaction.

Biogena fit@work® Stressbiotic is a natural, gentle and effective combination preparation containing lactobacteria, saffron extract and vitamins. It is suitable for relieving symptoms of stress-related IBS.

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