Towards psychobiotics for stress physiology & cognition: Bifidobacterium longum 1714 blocks stress-induced behaviour and physiology and modulates brain activity and neurocognitive performance in healthy human subjects

Andrew P. Allen, William Hutch, Yuliya E. Borre, Paul J. Kennedy, Andriy Temko, Geraldine Boylan, Eileen Murphy, John F. Cryan, Timothy G. Dinan, Gerard Clarke

1. Introduction

There is increasing interest in targeting the gut microbiome to affect brain and behavior in humans. Psychobiotics, probiotics that confer a mental health benefit upon the host, represent one such strategy [1]. There is existing evidence that chronic administration of multistrain probiotics or fermented milk probiotic products can impact upon the psychological and physiological indices of stress in humans [2], as well as upon central nervous system activity [3] and cognitive performance [4]. However, most of the evidence for psychobiotics comes from animal studies, and there has been a lack of translational selection of strains from preclinical screening to use in human studies. Previous research from our group has indicated that Bif longum 1714 can reduce the stress-related behaviours and improve memory performance in mice [5,6]. We thus investigate the impact of Bif longum 1714 on stress, resting brain activity and neurocognitive performance in healthy volunteers.

2. Aims & Hypothesis

Aim: Investigate the impact of Bif longum 1714 on stress, cognition and resting brain activity. Hypothesis: Bif longum 1714 would (a) reduce daily stress, (b) attenuate the psychological and physiological response to a controlled, acute stressor, (c) improve cognitive performance and (d). enhance brain activity.

3. Methods

Procedure

Daily stress: Daily stress was assessed using the Cohen Perceived Stress Scale. Participants completed this via an online survey administered with LimeSurvey software.

Neurocognitive performance: Participants completed the paired associates learning task (PAL), emotional recognition task and rapid visual information processing tests from the CANTAB platform; the PAL is associated with hippocampal activity (see Figure 3A).

Electroencephalography: Resting EEG for 5 minutes was assessed using the Compumedics Neuroscan® Stim system (see Figure 3B).

Acute stressor: Participants completed the socially evaluated cold pressor test (SECP; see Figure 4). Participants submerged their hands in water at 0-4°C for up to three minutes, while being evaluated by an cold and unencouraging confederate. Saliva samples for cortisol analysis were taken before and after stress exposure.

Figure 1 (Adapted from [7]): The brain and gut microbiota can communicate through various bidirectional routes.

Figure 2: Study timeline

Figure 3: Neurocognitive assessment: (A) CANTAB (B) EEG.

Figure 4: Socially evaluated cold pressor (SECP)

Figure 5: Brain and gut microbiota can communicate through various bidirectional routes.

Figure 6: Salivary cortisol (A) In response to SECP. (B) Area under the curve for each condition.

Figure 7: State anxiety pre- and post-stressor.

4. Results

Participants

Healthy male volunteers (N = 22) were recruited (see Table 1). Exclusion criteria were: having a significant acute or chronic illness, a condition, following a diet or taking a medication that would interfere with study objectives or pose a safety risk; English not participant's first language; smoking; habitually taking any probiotic products; any treatment involving experimental drugs warranted in the treatment of a medical condition; any treatment involving experimental drugs registered or in development; daily intake of probiotics (for example, yoghurt); history of drug or alcohol addiction in the last 5 years; in regular contact with people who use illegal drugs; neurological or psychiatric disorder; history of previous suicide attempts or self-harm; history of alcoholic or drug-related problems; history of depression; history of drug or alcohol dependence; recent use of a recreational drug or alcohol; or any condition or illness (other than those listed above) which in the opinion of the investigator would contraindicate participation in the study. The study was approved by the local ethics committee and all participants provided their written informed consent.

Daily stress

Daily stress was marginally lower at week 4 of the probiotic condition compared to placebo, t(18) = 1.95, p = .07, and increased again at follow-up (see Figure 5A). Overall stress was lower in the 1714 condition compared to placebo, t(18) = 2.32, p = .03 (see Figure 5B).

Acute stress response

The socially evaluated cold pressor increased cortisol cortisol at visits 0p < .001 (see Figure 6A). Bif longum 1714 reduced cortisol output in comparison to placebo and visit 1, t(21) = 8.67, p < .005 (see Figure 6B).

Cortisol

Figure 8: Paired associates learning total errors

Participants had higher mobility at Fz post-1714 compared to post-placebo or visit 1, t(21) = 13.37, p < 0.01 (see Figure 9A). Theta at Cz was lower post-1714 compared to post-placebo, t(21) = 10.31, p < 0.01 (see Figure 9B).

Figure 9: Resting EEG (A) EEG Mobility at Fz (B) Theta power at Cz.

5. Discussion & Conclusions

- The 1714 strain attenuated acute stress response to the socially evaluated cold pressor test, which elevated cortisol levels at all visits.
- Consumption of this strain lowered reported daily stress.
- Consumption of this strain is associated with subtle enhancements in visuospatial memory on a paired associates learning task.
- Frontal mobilization was enhanced and midline theta was reduced post-1714.
- The current research translates psychobiotic findings from preclinical research to healthy human volunteers.
- Further research is warranted to examine the impact of this psychobiotic strain in stress-related disorders.

References