THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 17, Number 5, 2011, pp. 427–434

DOI: 10.1089/acm.2010.0143

Ingested Oat Herb Extract (*Avena sativa*) Changes EEG Spectral Frequencies in Healthy Subjects

Wilfried Dimpfel, PhD,[1] Charlotte Storni, BSc,[2] and Marian Verbruggen, PhD[2]

Abstract

Objective: This study aimed at using quantitative assessment of human electric brain activity during mental work for determining acute effects of ingested oat herb extract on cognitive performance.
Design: Within a double-blind, randomized, placebo-controlled crossover study, two dosages of a special oat preparation of *Avena sativa herba* (1250 or 2500 mg of Neuravena®) were compared to placebo. An electroencephalogram was recorded while the patient had eyes open for 6 minutes, eyes closed for 4 minutes, performance of a concentration test (d2) for 5 minutes, and performance of mental arithmetic (KLT) for 5 minutes. Source density was calculated and spectral frequency changes were averaged to give one value for each frequency range.
Results: Using quantitative brain mapping technology (CATEEM®), main effects were observed in the left frontotemporal area, known to be involved in cognitive tasks. Statistically significant differences were observed during resting (lowering of spectral δ power) and during performance of the d2-concentration test (enhancement of spectral θ power) ($p < 0.01$ and $p < 0.05$, respectively). Also, during performance of mental arithmetic, greater enhancement of θ power was observed but only at a lower error probability ($p = 0.115$). No effects could be seen using the P300 paradigm during presentation of a visual stimulus.
Conclusions: These changes suggest that oat herb extract might be effective in healthy subjects, resulting in a positive impact on cognitive performance.

Introduction

Traditionally, green oat preparations have been used to support cognitive health since the Middle Ages. As reported by various monographs, preparations of *Avena sativa* herb have been traditionally used to reduce symptoms of acute and chronic anxiety and tension, stress and excitation, as well as neurasthenia, although the effectiveness for the claimed applications is not documented.[1]

The special wild green oat herb extract (Neuravena®) has been developed by screening for bioactivity, resulting in a specific high inhibition of monoamine oxidase B (MAO-B) as well as phosphodiesterase 4 (PDE-4), and standardized on the content of flavonoids such as isovitexin.[2] The above-mentioned central nervous system enzymes are known to be closely related to mental health and cognitive function. In a first, small preclinical study, the electric activity of the brain was recorded in four freely moving rats during 5 hours by means of measuring the field potential in electropharmacograms (principles of the methods are described in Dimpfel[3]). This assay revealed acute changes of brain activity after 20–50 minutes following a single administration of 100 mg/kg of Neuravena.® Results were interpreted to be in line with positive effects on cognitive function (preliminary unpublished results). Furthermore, a first indication that the abovementioned oat herb extract might be able to act directly on the communication structure of the brain was obtained with a behavioral study in rats.[4] In this 8-week study, comprising two different dosages of the oat herb extract and placebo, rats were subjected to different behavioral test-settings. Results showed that the extract was able to improve general learning performance, seemingly due to an enhanced alertness and improved stress coping abilities.

The above suggests that oat herb might contain ingredients acting directly on the communication structure of the brain related to cognitive performance. In order to assess possible direct effects of ingested oat herb extract on the human brain, it was decided to use quantitative measurement of the electric activity of the brain of healthy subjects after ingestion of two different dosages of this special prep-

[1]Justus Liebig University Giessen, Wetzlar, Germany.
[2]Frutarom Switzerland Ltd., Wädenswil, Switzerland.

aration in comparison to placebo. For quantitative evaluation of the electric brain activity, three neurophysiologic methods were applied: (1) quantitative electroencephalogram (EEG) in relaxed state,[5] (2) quantitative EEG during mental pressure, and (3) recording of visually evoked P300.[6] All methods have already been used for the description of effects on the brain induced by synthetic drugs as well as herbal medicines.[7–9] For the assessment of cognitive and emotional brain action, quantitative EEG has emerged as a reliable, easy-to-handle methodology, especially in its form of current density evaluation, which corresponds in its result to magnetencephalography. Recording of the P300 has been described in more than 1000 publications and has been related physiologically and pathophysiologically to attentive behavior.[10,11]

Materials and Methods

Subjects

Twenty (20) healthy volunteers (males and females) participated in this study. All subjects were between 30 and 60 years old (average 46.5±8.2 years). Subjects reporting neurological disturbances of the central nervous system (using *Diagnostic & Statistical Manual* 3rd edition) were excluded from the study. Subjects with a history of drug or ethanol abuse or participation in another study within the last 6 months were also excluded. Before initiation of the trial, it was ensured that they were not drinking alcohol. The subjects were familiarized with the tests during the initial period of the session. The interval between 2 experimental days was 1 week. On the day of the examination, no beverages containing caffeine were allowed within the last 12 hours preceding the EEG recording. The study was carried out according to the declaration of Helsinki (2000) on human rights. Procedures of good clinical practice testified by local authorities (Regierungspräsidium Darmstadt) were followed strictly. All subjects were informed about the goals of the study in detail and gave their written informed consent to participate. Subjects were randomly allocated to either one of the active drinks (containing 1250 or 2500mg of the oat herb extract) or placebo within a double-blind crossover design.

Test preparation

The wild green oat herb extract was obtained from Frutarom Switzerland Ltd. (Neuravena,® EFLA®955). Dried aboveground parts of a selected variety of *A. sativa* L.[2] underwent an extraction by using aqueous ethanol (30% w/w), were filtered according to a patented filtration process to remove lipophilic contaminants, concentrated, and spray-dried. *Maltodextrinum Ph.Eur*. 28% (w/w) was added as a carrier together with 2% (w/w) of silica *colloidalis anhydrica Ph.Eur*. Characteristics of the extract are a drug to extract ratio of 3.5:1, a flavonoid content (calculated as isovitexin) of ≥0.3% (w/w), and half of the maximal inhibitory concentration values (IC_{50}) of <200 μg/mL for *in vitro* inhibition of both MAO-B and PDE-4. Two different dosages (1250 mg = lower dosage and 2500 mg = higher dosage) of this extract were administered in comparison to placebo. The extract was dissolved in 100 mL of water. Then, 100 mL of orange juice (Fa. Müller, Germany) was added. For the placebo preparation, 100 mL of water was mixed with orange juice. To control for different color in comparison to placebo, 20 mg cacao powder was added to every drink. This amount is too low to interfere with the test.

Experimental procedures

EEG recording. The EEG was recorded bipolarly from 17 surface electrodes according to the international 10/20-system with Cz as physical reference electrode (**C**omputer-**a**ided **t**opographical **e**lectro**e**ncephalo**m**etry: CATEEM® from MediSyst GmbH, Linden, Germany) using an electrocap. For details refer to Schellenberg et al.[8]

Using a Lagrange interpolation, signals from 82 additional virtual electrodes were calculated to provide high-resolution topographical maps. The signals of all 99 electrode positions (17 real and 82 virtual) underwent the fast Fourier transformation based on 4-second sweeps of data epochs (Hanning window). Data were analyzed from 1.25 to 35 Hz using the CATEEM® software (NeuroCode AG). In this software, the resulting frequency spectra are divided into six frequency bands: δ (1.25–4.50 Hz), θ (4.75–6.75 Hz), α1 (7.00–9.50 Hz), α2 (9.75–12.50 Hz), β1 (12.75–18.50 Hz) and β2 (18.75–35.00 Hz). This frequency analysis is based on absolute spectral power values. Color coding of the maps is achieved by transforming the content of the power spectrum into spectral colors with a resolution of 0.25-Hz segments giving 140 frequency ranges. Additive mixture of these segments results in the final color display in the maps. Thus, frequency dependent focal changes of electric power result in local changes of color. Using this approach, it is possible to visualize spectral frequency changes taking place during the performance of mental tasks in comparison to the relaxation state (staring at the wall or fixing a point at the dark monitor). In this way a differential map can be calculated, which shows the change in frequency content at all electrode positions including the virtual ones derived from LaGrange interpolation between the physical electrode positions. Thus, a rather complete view can be given from electric changes represented by spectral colors, which are related to task. They represent the true proportions of frequency changes with respect to topographical distribution.

Data acquisition and analysis were carried out simultaneously and provide topographical maps displayed online. The maps show the relative, time averaged changes of electric brain activity of each specific recording condition in comparison to the reference period at the beginning.

Testing conditions. The concentration test (d2) is a well-known, standardized, validated test.[12] An arithmetic test (Concentration Performance Test [CPT]) was carried out as described in Smith et al.[13] Visual evoked potential P300 test was carried out as described in Dimpfel and Schober.[14]

Subjects were sitting alone in a quiet separate room with dimmed light in a comfortable chair. Baseline recording for 6 minutes under the condition eyes open was followed by recording for 4 minutes under the condition eyes closed. The next experimental period consisted of performing a concentration test (d2-test) followed by an arithmetic test (CPT). Finally, a visually P300 evoked potential was performed. All recordings were repeated in hourly intervals thereafter up to the 4th hour after ingestion of the test preparations. Between the measurements, subjects spent time in the facility's recreation room. All experiments took place at the same

time of day (starting at 7:00 AM). As the study design was crossover, volunteers visited the study center three times, with a washout period of at least 1 week.

Statistics. Since this study was an exploratory study with a small number of participants and EEG data are not normally distributed, the nonparametric sign test was chosen for comparison between placebo and treatment. Exploratory statistics gave p values, which are presented at the appropriate site.

Results

This study aimed at the quantization of cognitive features of brain electric activity. Therefore, not only was the whole brain analyzed under different conditions, but additionally special emphasis was put on the left frontotemporal electrode positions F3, F7 (frontal), and T3 (temporal) as these are the regions known to be involved in cognitive processing.

Effects of oat herb extract during general EEG recording

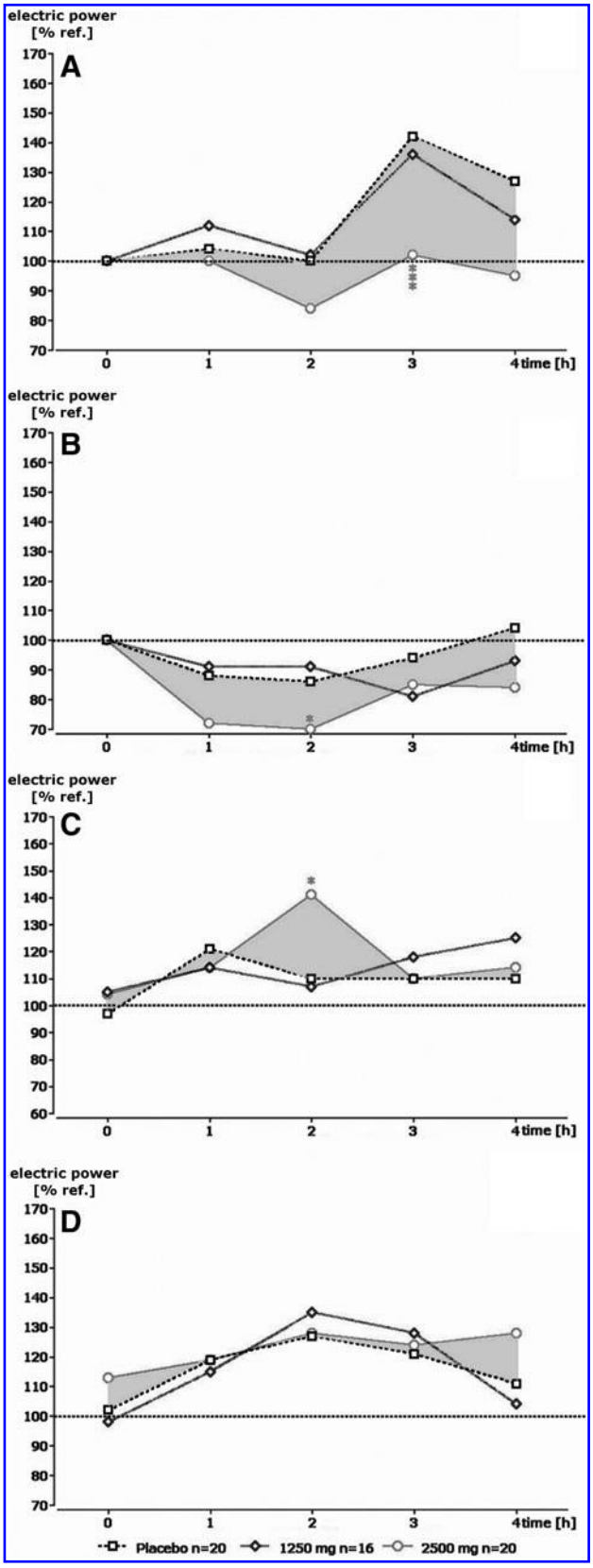
In order to see a potential general effect of oat herb extract on electrical brain activity, data from all electrode positions were averaged and related to baseline values, recorded before ingestion. An overview on the two conditions (eyes open and eyes closed) is given in Table 1. The ingestion of oat herb extract did not significantly change the general electric activity. Under the condition eyes open, there is an indication that circadian rhythm–dependent increase of θ and $\alpha 1$ power is prevented during the second hour after ingestion of the higher dosage ($p = 0.115$ and $p < 0.05$, respectively). Furthermore, $\alpha 2$ power slightly increased in comparison to placebo, during the fourth hour after ingestion of the higher dosage ($p = 0.115$). During the condition eyes closed, where the visual perception is disabled, δ and θ power values were clearly reduced compared to the values obtained with placebo, and reached statistical significance ($p < 0.05$) in the third and fourth hour after ingestion of the higher dosage.

Table 1. Electrical Power in Percent of the Baseline Values Recorded Before Ingestion of Two Dosages of Oats: 1250 mg and 2500 mg

Placebo time [h]	δ	p-*Value*	θ	p-*Value*	$\alpha 1$	p-*Value*	$\alpha 2$	p-*Value*	$\beta 1$	p-*Value*	$\beta 2$	p-*Value*
A All electrodes eyes open												
1	79.81		104.42		134.81		110.82		106.12		111.24	
2	73.39		117.26		150.55		117.41		115.62		116.70	
3	85.45		109.15		157.52		118.66		131.59		115.20	
4	92.19		132.49		160.77		119.46		119.27		106.72	
1250 mg time [h]												
1	78.89		104.49		129.34		114.87		109.76		106.85	
2	79.70		107.08		136.72		118.91		123.16		112.90	
3	77.93		105.93		158.24		125.25		125.34		106.02	
4	80.17		111.43		166.83		146.08		134.98		109.59	
2500 mg time [h]												
1	79.82		89.17		139.24		114.01		106.11		103.67	
2	72.20		92.18	0.115 ↓	122.90	0.041 ↓	123.05		118.12		110.71	
3	79.98		108.32		162.15		133.28		124.28		111.82	
4	82.27		108.81		167.43		137.68	0.115 ↑	125.89		111.42	
B All electrodes eyes closed												
1	102.29		128.17		118.50		96.80		118.10		94.11	
2	111.15		134.48		121.79		102.31		120.05		101.03	
3	142.91		153.23		128.24		99.34		135.59		97.76	
4	129.64		141.83		130.69		99.43		132.62		106.67	
1250 mg time [h]												
1	102.48		119.53		122.41		127.39		115.72		95.92	
2	106.19		134.18		138.52		113.88		127.22		107.03	
3	99.95		141.42	0.077 ↓	156.23		118.78		124.66		103.28	
4	105.57		161.42		152.40		139.93		139.82		116.08	
2500 mg time [h]												
1	93.09		114.71		103.62	0.115 ↓	107.18		106.34		98.56	
2	86.25		128.67		110.42		110.43		116.25		94.46	
3	90.55	0.041 ↓	128.27	0.115 ↓	124.31		115.66		122.51		102.57	
4	92.16		117.21	0.012 ↓	128.42		104.37		116.90		97.69	

Data are given as median of all 17 electrode positions. Statistical significance in comparison to placebo is given as p-value. Direction of change is indicated by arrows.

The results of the activity in the left frontotemporal region show a similar picture (Figures 1 and 2 top). During the condition eyes closed (Fig. 1A), circadian increases of δ power were completely prevented during the recording time for the higher dosage, but no difference could be shown for the lower dosage. During the third hour after ingestion, the value obtained with the higher dosage was highly statistically significantly different from placebo. A similar picture arose during the recording condition eyes open (Fig. 1B). Delta power values were always lower for the higher dosage of oat herb extract compared with placebo, but only during the second hour a statistical tendency was seen. Evaluation of θ power at these electrode positions revealed a tendency to a general decrease of power after ingestion of the higher dosage for both conditions eyes open and eyes closed (Fig. 2A and B).



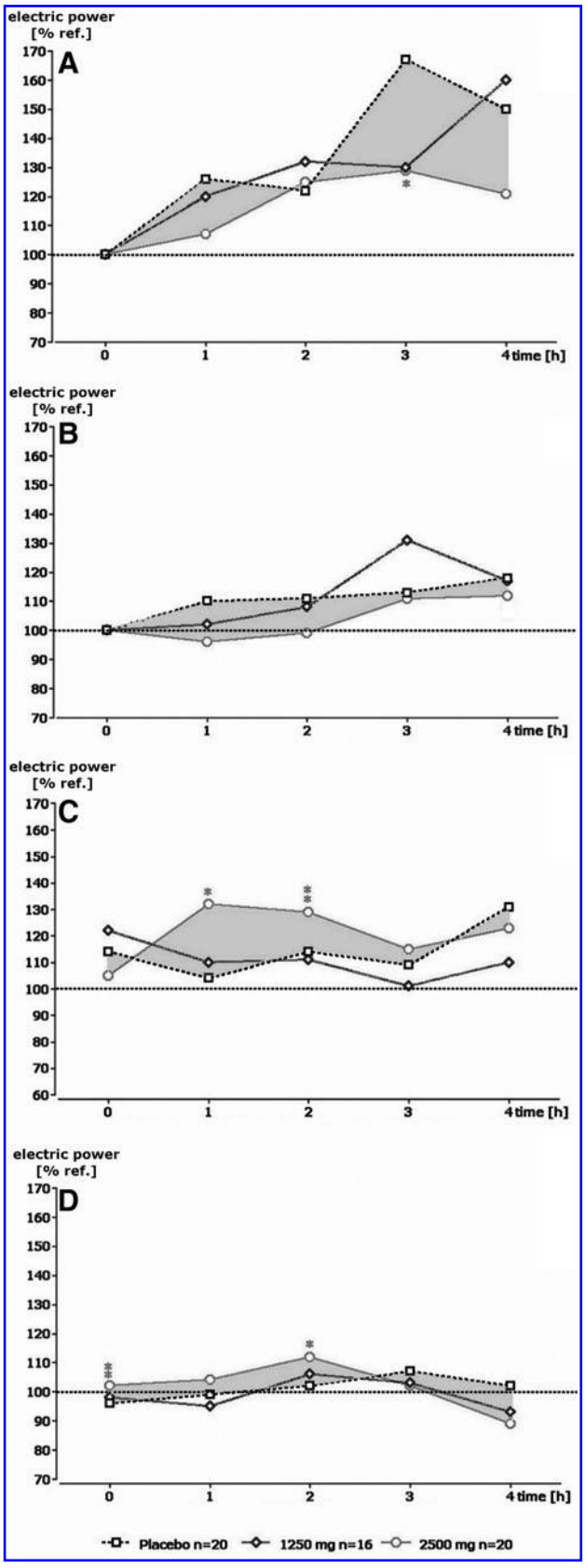
Effects of oat herb extract during mental performance

For quantitative evaluation of electric changes during mental performance, the median of the three positions F7, F3, and T3 was calculated[15] (Table 2) and results were compared with baseline results for the condition eyes open (Figs. 1 and 2, bottom). The suggested frequencies and brain areas have been shown to be important during performance of working memory tasks also by other authors[16,17] and also during other cognitive tests, such as sentence processing.[18]

During performance of the d2-test an increase in δ activity, in comparison to placebo, was seen during the second hour after ingestion of the higher dosage ($p = 0.115$), a trend that is close to statistical significance (Fig. 1C). Furthermore, θ power tended to increase during the first and second hour of performance of the d2-test after ingestion of the oat herb extract ($p = 0.115$ and $p < 0.05$, respectively; Fig. 2C). During performance of the mental arithmetic test (CPT), no significant changes of electric pattern could be observed, except for a tendency of increased θ power during the second hour after administration (Fig. 2D).

A different way to look at the communication structure of the brain is to transform the result of the frequency analysis into spectral colors (see Methods; Fig. 3). The change of the electric pattern due to performance of the d2-concentration test under placebo condition is shown in part A, in comparison to those in the presence of the higher dosage of oat herb extract, part B. Focusing on the left frontotemporal cortex (marked by a circle) more red color is depicted in this area in the presence of the higher dosage. This finding is presumably due to a more orange-appearing θ power (circles at the bar graphs) and an increase of blue β power. There was also a decrease in $\beta 2$ power at the electrode positions T5

FIG. 1. Time course of changes in δ activity for median of frontotemporal electrode positions F7, F3, and T3. Values on the ordinate are given in percent of the pre-administration baseline values at the particular timing. **A.** Recording condition "eyes closed." **B.** Condition "eyes open." **C.** Values on the ordinate as recorded during performance of the d2-test with reference to eyes open at the particular timing. **D.** Values on the ordinate as recorded during performance of the concentration-performance test with reference (ref.) to eyes open at the particular timing. Statistically significant differences are marked as asterisks: *Trend to significance; ***$p < 0.01$ error probability.



and T6. The other brain areas showed very similar frequency changes under these experimental conditions (for example, centroparietal decreases in α power), but no difference between placebo and oat herb extract. The change due to performance of the mental arithmetic test (CPT) under placebo is shown in part C, in comparison to those in the presence of the higher dosage, part D. The appearance of the frontal area is somewhat different in the CPT, in comparison to the changes in the presence of the d2-concentration test. For example, in the CPT the increase of temporal beta activity can be observed to a lesser extent. Thus, the method is sensitive enough to discriminate between the accompanying electrical features of two different psychometric tests. Focusing on the left frontal area (marked by a circle), more red color is visible in the presence of oat herb extract than under control conditions. This is due to higher δ and θ activity, especially on the electrode position F7 and T3 (marked by a circle).

Visually evoked potential

Evaluation of the recording results of the visually evoked P300 potential did not reveal a difference between the two oat preparations and placebo (details not shown).

Discussion

The present investigation aimed at the detection of spectral frequency changes of electric brain activity as an indication of better cognitive performance after ingestion of oat herb extract. Although the results do not completely prove this assumption, they provide solid evidence that within an acute study design, cognitive performance–related electric changes, obtained after ingestion of different dosages of an oat herb extract, differ from placebo. The direction of changes that became statistically significant from control are in line with an improvement of at least the concentration task, since increases of θ power during performance of mental tasks have been related to better mental fitness in earlier studies.[5] Therefore, taking into account the limitations of a rather small study population to reach statistical significance, the current study can be considered first proof that oat herb extract influences human brain activity during performance tasks, and supports the obtained positive effects with regard to behavioral changes after subchronic treatment of rats with the oat herb preparation.[4]

FIG. 2. Time course of changes in θ activity for median of frontotemporal electrode positions F7, F3, and T3. Values on the ordinate are given in percent of the pre-administration baseline values at the particular timing. **A.** Recording condition "eyes closed." **B.** Condition "eyes open." **C.** Values on the ordinate as recorded during performance of the d2-test with reference to eyes open at the particular timing. **D.** Values on the ordinate as recorded during performance of the concentration-performance test with reference (ref.) to eyes open at the particular timing. Statistically significant differences are marked as asterisks: *Trend to significance; **$p < 0.05$ error probability.

Table 2. Electrical Power in Percent of the Reference Values (Eyes Open) as Recorded After Ingestion of Two Dosages of Oats: 1250 mg and 2500 mg in Comparison to Placebo

Placebo time [h]	*δ*	p-*Value*	*θ*	p-*Value*	*α1*	p-*Value*	*α2*	p-*Value*	*β1*	p-*Value*	*β2*	p-*Value*
A Electrodes F7, F3, T3 d2-test												
1	120.94		103.80		97.84		96.03		113.82		108.87	
2	110.48		113.48		84.39		95.92		100.35		89.47	
3	110.34		108.60		95.12		89.83		95.43		99.93	
4	110.21		130.74		94.49		98.49		102.97		103.94	
1250 mg time [h]												
1	113.74		110.43		106.32		99.64		114.34		128.86	
2	106.50		111.23		92.70	0.077 ↑	107.11		112.13		132.92	
3	117.76		100.79		102.47		102.13		102.36		97.56	
4	124.97		109.61		111.15		104.56		123.29	0.021 ↑	127.54	
2500 mg time [h]												
1	113.56		131.98	0.115 ↑	89.09		95.06		109.57		111.20	
2	140.95	0.115 ↑	128.45	0.041 ↑	93.78	0.115 ↑	94.50		111.66		109.04	
3	109.63		115.39		71.27		99.44		104.60		101.14	
4	114.22		123.18		79.82		91.90		110.30		120.53	0.115 ↓
B Electrodes F7, F3, T3 CPT												
1	118.39		99.22		67.60		79.15		88.60		80.08	
2	127.15		101.72		59.89		71.83		68.91		70.94	
3	121.27		107.23		74.50		74.12		74.83		73.01	
4	110.46		102.02		66.61		71.78		75.43		80.04	
1250 mg time [h]												
1	114.96		95.25		73.79		80.07		78.76		88.41	0.077 ↑
2	135.43		105.56		67.44		79.74		69.18		69.87	
3	128.40		102.55		77.70		81.96		88.59		100.69	
4	103.88		93.02		84.46		78.27		82.97	0.077 ↑	98.05	0.077 ↑
2500 mg time [h]												
1	118.52		104.23		64.17	0.041 ↑	77.97		87.48		94.52	
2	128.04		112.10	0.115 ↑	59.31		71.16		79.89		84.54	
3	123.96		102.07		64.88		76.07		91.03		86.80	0.115 ↑
4	127.60		89.05		58.11		71.55		88.46		77.52	

Data are given as median of frontotemporal electrode positions. Statistical significance in comparison to placebo is given as *p*-value. Direction of change is indicated by arrows.

CPT, Concentration Performance Test.

Delta activity

The interpretation of frequency changes in the EEG has made remarkable progress in terms of neurotransmitters involved as well as human behavior. Especially from investigations in rats, it became obvious that δ activity of field potentials seems to be modulated by the cholinergic transmitter system,[19] which is involved in cognitive processing. The observed decrease of baseline activity under the condition eyes open can therefore be regarded as a better prerequisite for mental performance. This finding could be confirmed through a significantly different increase in δ activity, compared with placebo, during the performance tests.

Theta activity

Theta activity could be shown to be modulated by compounds acting on the noradrenergic $\alpha 2$ receptor.[14] Frontal θ power is associated with states of focused concentration, and its enhancement might reflect conscious control over attention with maintenance of a task-appropriate mental set.[13] Furthermore, it is known that patients with dementia produce considerably less δ and θ activity during mental work due to a higher baseline level at rest.[20] The direction of changes that became statistically significant from control are in line with an improvement of at least the concentration task, since increases of θ power during performance of mental tasks have been related to better mental fitness in earlier studies.[21] Task-related increases of frontal θ power in the presence of oat herb extract can therefore be regarded as a reliable parameter of better performance.

With respect to possible reasons for the regional specificity, one can only speculate that one or more constituents of the extract have a high affinity to particular ion channels or neurotransmitter receptors controlling the activity of these ion channels and signal transduction in the frontal brain region. Since the activity of these ion channels set the regional activity pattern in the form of field potentials

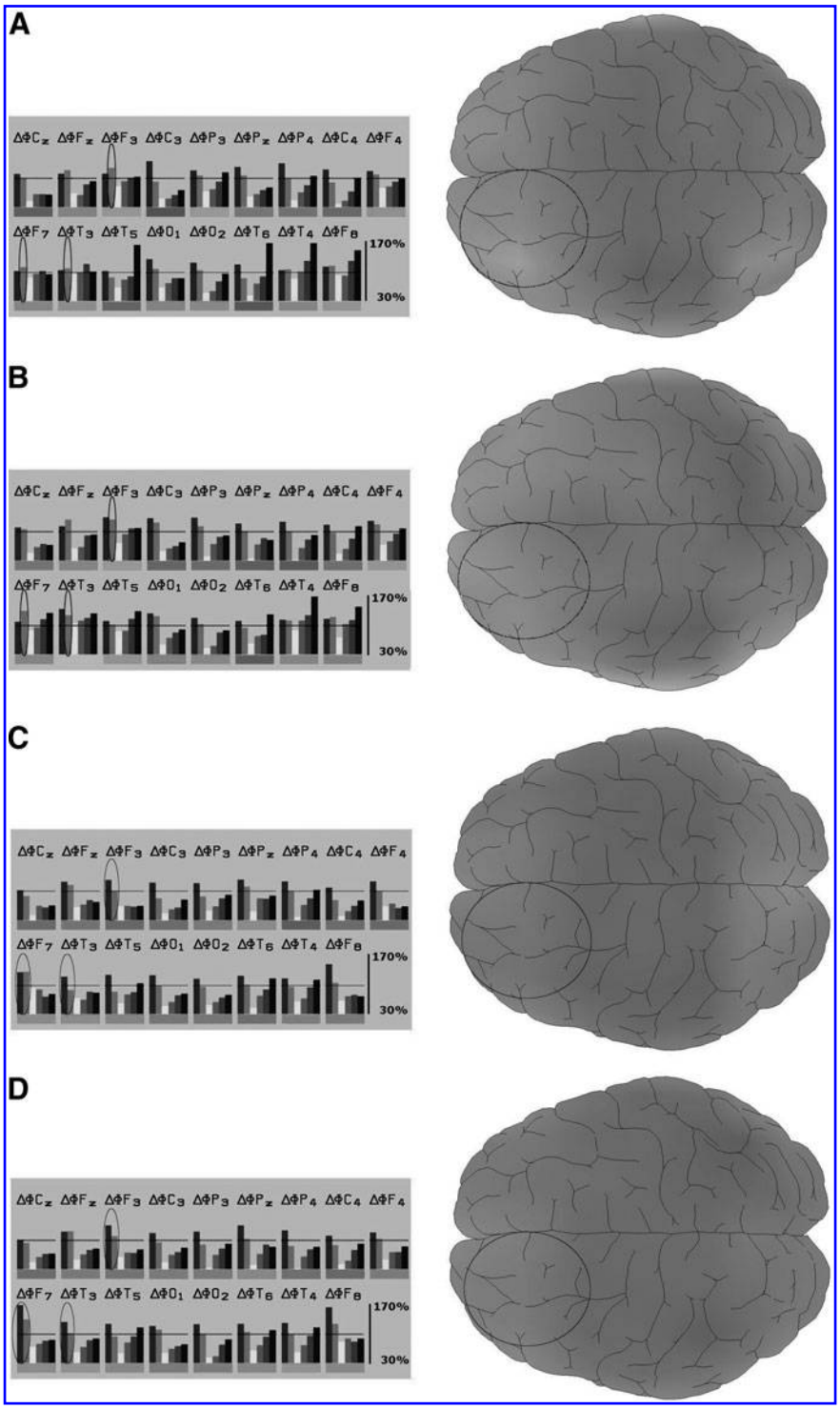


FIG. 3. Brain map depicting local changes of spectral frequency power transformed into spectral colors (for details see Methods section) at 2 hours after ingestion. Differences between placebo and the higher dosage are marked by circles (big circles within the map and small circles emphasizing changes at single electrode positions within the bar graph. **A.** Average map in the presence of placebo during the performance of the d2-test. **B.** Average map in the presence of the higher dosage during the performance of the d2-test. **C.** Average map in the presence of placebo during the performance of mental arithmetics (CPT). **D.** Average map in the presence of the higher dosage during the performance of mental arithmetics (CPT).

(reflected within the EEG of humans), local differences in brain electric activity are to be expected to change in the presence of receptor or ion channel modulation chemicals. One example for cholinergic modulation by an herbal preparation (lemon balm) is given in the literature.[22] According to these authors, interference of a special extract with cholinergic transmission led to changes in cognition and mood.

Conclusions

In conclusion, the above-discussed brain activity observations suggest that a single supplementation with oat herb extract may affect mental fitness in healthy volunteers. This hypothesis, as well as the possible effects of a long-term application of the extract, should be further studied in suitable cognitive models.

Acknowledgments

We cordially thank Mrs. Petra Werling for performance of the experiments and Mrs. Leonie Schombert for documentation of the results.

Disclosure Statement

This study was initiated and performed by Neurcode AG, with financial support of Frutarom Switzerland Ltd., CH-8820 Wädenswil, Switzerland. The co-authors M. Verbruggen and C. Schellekens are employed by Frutarom, but have had no influence on the design of the study. No competing personal financial interest exists.

References

1. Klein J, Blumenthal M, eds. The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines. Austin: American Botanical Council, 1998:356–356.
2. Moccetti T, Wullschleger C, Schmidt A, et al. Bioactivity-based development of a wild green oat (Avena Sativa L) extract in support of mental health disorders. Z Phytother 2006;27:24.
3. Dimpfel W. Preclinical data base of pharmaco-specific rat EEG fingerprints (Tele-Stereo-EEG). Eur J Med Res 2003;8: 199–207.
4. Schellekens C, Perrinjaquet-Moccetti T, Wullschleger C, Heyne A. An extract from wild green oat improves rat behaviour. Phytother Res 2009;23:1371–1377.
5. Saletu B. The use of pharmaco-EEG in drug profiling. In: Hindmasch, Stonier P, eds. Human Psychopharmacology: Measures and Methods, Vol. 1. Chichester: Wiley, 1987:173–200.
6. Sutton S, Braren M, Zubin J, John ER. Evoked-potential correlates of stimulus uncertainty. Science 1965;150:1187–1188.
7. Dimpfel W, Todorova A, Vonderheid-Guth B. Pharmacodynamic properties of St. John's Wort. A single-blind neurophysiological study in healthy subjects comparing two commercial preparations. Eur J Med 1999;4:303–312.
8. Schellenberg R, Sauer S, Dimpfel W. Pharmacodynamic effects of two different hypericum extracts in healthy volunteers measured by quantitative EEG. Pharmacopsychia 1998;31:44–53.
9. Dimpfel W, Pischel I, Lehnfeld R. Effects of lozenge containing lavender oil, extracts from hops, lemon balm and oat on electrical brain activity of volunteers. Eur J Med Res 2004;9:423–431.
10. Werber EA, Gandelman-Marton R, Klein C, Rabey JM. The clinical use of P300 event related potentials for the evaluation of cholinesterase inhibitors treatment in demented patients. Neural Transm 2003;11:659–669.
11. Polich J. Clinical application of the P300 event-related brain potential. Phys Med Rehabil Clin N Am 2004;15:133–161.
12. Brickenkamp R, Zillmer E. D2 Test of Attention. Toronto: Hogrefe & Huber Publishing, 1998.
13. Smith ME, McEvoy LK, Gevins A. Neurophysiological indices of strategy development and skill acquisition. Brain Res Cogn Brain Res 1999;7:389–404.
14. Dimpfel W, Schober F. Norepinephrine, EEG theta waves and sedation in the rat. Brain Pharmacol 2001;1:89–97.
15. Klimesch W. EEG alpha and theta oscillations reflect cognitive and memory performance: A review and analysis. Brain Res Rev 1999;29:169–195.
16. Onton J, Delorme Makeig S. Frontal midline EEG dynamics during working memory. Neuroimage 2005;27:341–356.
17. Sauseng P, Klimesch W, Doppelmayr M, et al. Theta coupling in the human electroencephalogram during a working memory task. Neurosci Lett 2004;354:123–126.
18. Hald LA, Bastiaansen MCM, Hagoort P. EEG theta and gamma responses to semantic violations in online sentence processing. Brain Language 2006;96:90–105.
19. Dimpfel W. Pharmacological modulation of cholinergic brain activity and its reflection in special EEG frequency ranges from various brain areas in the freely moving rat (tele-stereo-EEG). Eur Neuropsychopharmacol 2005;15:673–682.
20. Schellenberg R, Todorova A, Hofmann HC, et al. Differentiation of demented patients and healthy subjects by means of quantitative-topological EEG: A classification approach. Alzheimer's Res 1995;1:23–28.
21. Schober F, Schellenberg R, Dimpfel W. Reflection of mental exercise in the dynamic quantitative topographical EEG. Neuropsychobiology 1995;31:98–112.
22. Kennedy DO, Wake G, Savelev S, et al. Modulation of mood and cognitive performance following acute administration of single doses of Melissa officinalis (lemon balm) with human CNS nicotinic and muscarinic receptor-binding properties. Neuropsychopharmacology 2003;28:1871–1881.

Address correspondence to:
Charlotte Storni, BSc
Frutarom Switzerland Ltd.
Rütiwisstrasse 7
Wädenswil CH-8820
Switzerland

E-mail: cstorni@ch.frutarom.com