Changes of Clinically Important Neurotransmitters under the Influence of Modulated RF Fields—A Long-term Study under Real-life Conditions

Klaus Buchner and Horst Eger

This follow-up of 60 participants over one and a half years shows a significant effect on the adrenergic system after the installation of a new cell phone base station in the village of Rimbach (Bavaria). After the activation of the GSM base station, the levels of the stress hormones adrenaline and noradrenaline increased significantly during the first six months; the levels of the precursor dopamine decreased substantially. The initial levels were not restored even after one and a half years. As an indicator of the dysregulated chronic imbalance of the stress system, the phenylethylamine (PEA) levels dropped significantly until the end of the study period.

The effects showed a dose-response relationship and occurred well below current limits for technical RF radiation exposures. Chronic dysregulation of the catecholamine system has great relevance for health and is well known to damage human health in the long run.

Keywords: cell phone base station, long-term study, stress hormones, radiofrequency radiation, GSM transmitter, far-field radiation

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Introduction

Despite the distribution of numerous wireless transmitters, especially those of cell phone networks, there are only very few real-life field studies about health effects available. In 2003, the Commission on Radiation Protection was still noticing that there are no reliable data available concerning the public’s exposure to UMTS radiation near UMTS base stations (1).

Since the 1960s, occupational studies on workers with continuous microwave radiation exposures (radar, manufacturing, communications) in the Soviet Union have shown that RF radiation exposures below current limits represent a considerable risk potential. A comprehensive overview is given in the review of 878 scientific studies by Prof. Hecht, which he conducted on behalf of the German Federal Institute of Telecommunications (contract no. 4231/630402) (2, 3). As early as the 1980s, US research projects also demonstrated in long-term studies that rats raised under sterile conditions and exposed to "low-level" RF radiation showed signs of stress by increased incidences of endocrine tumors (4, 5).

Concerned by this "scientific uncertainty" about how radiofrequency “cell tower radiation" affects public health, 60 volunteers from Rimbach village in the Bavarian Forest decided to participate in a long-term, controlled study extending about one and a half years, which was carried out by INUS Medical Center GmbH and Lab4more GmbH in
Common risk factors such as external toxic agents, parameters of the catecholamine system (6) were determined prior to the activation of the GSM transmitter and followed up in three additional tests for a period of more than 18 months. The informed consent of all participants included the condition that the data were to be published anonymously.

Materials and Methods

Study Setting and Selection of Study Subjects

In spring 2004, a combined GSMD1 and GSMD2 cell transmitter (900 MHz band) was installed on Buchberg mountain in D-93485 Rimbach (Lower Bavaria) with two sets of antenna groups each. The installation height of the antennas for both systems is 7.9 m; the horizontal safety distance along the main beam direction is 6.3 or 4.3 m, respectively. At the same tower, there is also a directional antenna at 7.2 m (7).

Shortly after it had become known that the wireless transmitters were to be installed, all inhabitants of Rimbach had been asked to participate in a mass screening. The municipality has approximately 2,000 inhabitants. In 60 volunteers (27 male, 33 female) aged between 2 and 68, the levels of adrenaline, noradrenaline, dopamine, and PEA (phenylethylamine)—which cannot be consciously regulated—were determined in their urine at the end of January/beginning of February 2004 (shortly before the activation of the antennas and the RF emissions beginning) as well as in July 2004, in January 2005, and in July 2005.

Most of these study participants signed up immediately after an informational gathering in late January 2004, at which the course of action by the cell phone service providers was criticized. Others signed up following a call for participation in the local paper. Since Rimbach is a small municipality, mouth-to-mouth propaganda also played a role. Participation was made attractive to the volunteers because a lab test that usually would be very expensive was offered for a small fee. Since the study required to show the status of the biological parameters over a given time period, only those study subjects participating in all four tests are included.

The data presented below come primarily from volunteers who have a certain interest in the life of their community and their health. Other persons joined the stress hormone investigation because of the recommendation of, or request by, their fellow citizens. This does not meet the requirements for a random sample. The result of this study, however, is hardly affected because Rimbach is a very small municipality. Therefore, the social contacts that lead to participation are very important. Most probably they do not affect the blood parameters. Furthermore, numerous large families participating as a whole whereby the health status of the individual family members did not play any role. For this reason, but especially because of the population structure, the study includes many children but only a few adolescents and young adults: there are hardly any opportunities for occupational training in Rimbach. In contrast, the municipality is attractive to young families with many children.

Sample Collection

The second morning urine was collected at INUS Medical Center on Mondays between 9:00 and 11:00 a.m. We made sure that each participant’s appointment was always scheduled for the same time and that the time of breakfast or the state of fasting was the same for each participant at all tests. On the same day, the samples were sent by express to Labor Dr. Bieger in Munich where they were processed. In addition, samples were also sent to a laboratory in Seattle for control analyses (8–11).

Medical History

Medical doctors of the INUS Medical Center took a thorough medical history of each participant. At the initial test, the following data were also gathered: exact address, average time spent at home, indoor toxins, stress due to heavy-traffic roads, and the number of amalgam fillings. The latter number also included fillings that had already been removed. A nine-year-old child was noted to be electro-
sensitive to the effects of household wiring and connected appliances. All other study participants declared themselves to be not electro-sensitive.

When taking their medical history, participants were also questioned about subjective symptoms and chronic diseases at the start of the study and during its course; if overweight, this was also noted. In this study, overweight in adults is defined as a weight greater than the "body height in cm minus 100 plus 5 kg tolerance."

Consistency checks for the parameter "overweight," however, indicate that—especially with regard to children—different criteria have been applied during the taking of the medical history. These data, therefore, can only serve as a reference point. They are listed here anyhow since they can provide suggestions for further studies.

All atopic disorders such as:
1. Hay fever, neurodermatitis, allergies, asthma, eczema are referred to as "chronic disorders," as well as
2. All chronic inflammations such as interleukin- or COX-2-mediated problems;
3. All autoimmune diseases such as rheumatism, multiple sclerosis (MS);
4. All chronic metabolic disorders such as diabetes, liver diseases, intestinal diseases, kidney diseases.

Out of the 16 chronically affected participants 12 had allergies.

It was also asked whether there were DECT, Wi-Fi, or Bluetooth devices in the house or apartment during the study period from late January 2004 until July 2005. Also included were those devices present only for part of the study period, but not those turned off at night.

Exposure Level Measurements

For the most part, Rimbach municipality is located at one side of a narrow V-shaped valley. The cell phone base station is situated almost right across from the village center on the other side. RF radiation levels were measured at the outside of the residences of all study participants, wherever possible with direct line of sight of the transmitter. Because the municipality is located on a slope, great differences were noted inside homes—depending on whether or not a line of sight to the transmitter existed. In three cases, it was possible to measure the exposure levels at the head end of the bed. In these cases, the peak value of the power density was lower by a factor of 3.5 to 14 compared to measurements in front of the house with direct line of sight to the transmitter. The exact location of DECT, Wi-Fi, and Bluetooth base stations (if present) as well as possible occupational exposures, etc. were not determined by most participants.

At first, the measurements were taken with a broadband RF meter HF38B of Gigahertz Solutions, for which the manufacturer guarantees an error margin of max. ±6 dB (±7 decimal places; but this error can be mostly eliminated by selecting the appropriate measurement range). However, an inspection revealed that the error margin was less than ±3 dB. In addition, the broadband RF meter HF59B (±3 dB, ±5 decimal places) was used at several points. With this RF meter, relevant frequencies can be analyzed with variable filters, the ELF modulation frequencies via fast Fourier analysis.

By using broadband RF meters, the testing effort and expense are reduced compared to spectrum analyzers. Thus, it was possible to take measurements at a greater number of points, and as a result, it was easier to determine the maxima and minima of the power density levels. Furthermore, the accuracy of high-quality broadband RF meters is similar to that of spectrum analyzers.

In this study, only cell phone signals are considered: not DECT, Wi-Fi, or Bluetooth devices inside homes or emissions from broadcast or TV stations at Hohenbogen, a mountain above Rimbach. For the most part, the emissions from the latter transmitters remained stable during the study period, whereas the focus of this study is on changes in exposure levels. For almost all sample measurements, the portion of the exposure due to the transmitter at Hohenbogen was at maximum 35 µW/m² (peak value). It was higher in the residences of only two study participants: 270 µW/m² (average) or 320 µW/m² (peak), respectively. At these residences, the GSM exposure was approximately 10 µW/m².

For the assessment, the peak values of the signals are used because, in the case of GSM radiation, they are less dependent on the usage level than average values. The peak value of the power density for all study participants from Rimbach was on average 76.9 µW/m² (Tab. 1).

In Figure 1 the exposure of the participants is given as power density levels in increments of 30 µW/m².

Classification of Participant Group and Exposure Levels

Sixty persons participated in the study; their age distribution is shown in Figure 2 according to year groups. In order to capture the effect of the cell phone base station, other environmental factors must be excluded as much as possible. It is vitally important to ensure that no major differences between high-exposure and low-exposure persons influenced the results.
As shown in Table 1, the group with exposure levels greater than 100 µW/m² included fewer chronically ill persons and fewer residences at heavy-traffic roads, but considerably higher amalgam exposures by dental fillings compared to the average of the participants. These differences, however, cannot explain the observed development of the blood parameters as will be shown further below. It should also be noted that the number of children in the group of <= 60 µW/m² is considerably lower than in the other two groups.

**Statistics**

Because of the large individual differences in blood values, their asymmetrical distribution, and because of the many “outliers,” the assessment presented here focuses on the following problem: “Did the level of a given substance predominantly increase (or decrease, respectively) in the test subjects?” For this problem, the so-called signed-rank paired Wilcoxon test (12) is applied. How to determine the confidence intervals of medians is described in an easy-to-understand form in (13).

Due to the rather large differences in individual values, we refrained from carrying out additional statistical analyses, especially those with parametric methods.

**Results**

1 Clinical Findings

Adrenaline, noradrenaline, and dopamine as well as phenylethylamine (PEA) levels were determined at the time when the medical history was taken at INUS Medical Center. Out of the 60 participants, eleven had sleep problems until the end of 2004. During the study period (until July 2005), eight additional cases with these problems were reported. At the end of January 2004, only two participants complained about headaches; eight additional cases were reported thereafter. For allergies, there were eleven cases in the beginning and 16 later; for dizziness five and eight; and for concentration problems ten and fourteen. Due to the limited number of participants, no meaningful statements can be made about changes during the study period regarding the conditions tinnitus, depression, high blood pressure, autoimmune diseases, rheumatism, hyperkinetic syndrome, attention deficit hyperactivity disorder (ADHD), tachycardia, and malignant tumors. (Tab. 2)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Before activation of transmitter</th>
<th>After activation of transmitter</th>
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<tbody>
<tr>
<td>Sleep problems</td>
<td>11</td>
<td>19</td>
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<tr>
<td>Headache</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Allergy</td>
<td>11</td>
<td>16</td>
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<tr>
<td>Dizziness</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Concentration problems</td>
<td>10</td>
<td>14</td>
</tr>
</tbody>
</table>

Tab. 2: Clinical symptoms before and after activation of transmitter.
2 Adrenaline

The adrenaline level trends are shown in Figure 3. After the activation of the transmitter from January until July 2004, a clear increase is followed by a decrease. In participants in the exposure category above 100 µW/m², the decrease is delayed.

Since the distribution of the adrenaline levels is very asymmetrical as shown in Figure 4, the median values are better suited for evaluation than the average values. However, there is no significant difference between the trend of the median and the trend of the average values (Tab. 3). But it stands out that, in the lowest exposure group with a power density below 60 µW/m², median values do not decrease between July 2004 and January 2005.

The statement “The adrenaline values of study subjects increased after the activation of the transmitter, i.e. between January and July 2004” is statistically confirmed (p<0.002), as well as the statement “The adrenaline level of the study participants decreased from July 2004 to July 2005” (p<0.005). In the lowest exposure group, the increase is the smallest. Until the end of the study period, these values do not drop.

A certain dose-response relationship can be observed for the increase in adrenaline levels from January 2004 until July 2004. The increase in medians was 2.3 µg/g creatinine for all subjects. At an RF radiation level up to 60 µW/m², creatinine was 1.0 µg/g, and by contrast, for power density levels between 60-100 µW/m² it was 2.6 µg/g.

For subjects in the exposure group above 100 µW/m², creatinine levels were found to be 2.7 µg/g, i.e. this value did not increase. We refrain from any additional statistical analysis because, as shown further below, the increase in adrenaline levels was mainly observed in children and chronically ill participants whose numbers were not sufficient to be broken down into further subgroups.

<table>
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<td></td>
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<td>6.1 - 10.0</td>
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<td>7.4</td>
<td>7.8</td>
</tr>
<tr>
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<td>CI</td>
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<td>4.6 - 13.2</td>
<td>3.4 - 9.4</td>
</tr>
<tr>
<td>60-100 µW/m²</td>
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<td>10.4</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td>Median</td>
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<td>10.2</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>CI</td>
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<td>6.6 - 12.8</td>
<td>5.0 - 11.2</td>
</tr>
<tr>
<td>&gt;100 µW/m²</td>
<td>Average</td>
<td>8.9</td>
<td>12.0</td>
<td>11.1</td>
</tr>
<tr>
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<td>Median</td>
<td>8.2</td>
<td>10.9</td>
<td>10.6</td>
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<tr>
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<td>CI</td>
<td>5.3 - 10.9</td>
<td>5.7 - 19.6</td>
<td>5.8 - 15.2</td>
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</table>

Tab. 3: Results for adrenaline levels in µg/g creatinine
CI = 95% confidence interval of median

Fig. 3: Median adrenaline levels for all participating citizens of Rimbach whose cell phone base station exposure was above 100 µW/m², between 60 and 100 µW/m², or up to 60 µW/m². The power density levels refer to peak values of the GSM radiation exposure in front of a given residence.

Fig. 4: Distribution of adrenaline levels in µg/g creatinine

Fig. 5: Median adrenaline levels for all participating citizens of Rimbach who have a DECT phone, Wi-Fi, or similar device, for those who do not have such wireless devices, and for the lowest exposure group without indoor wireless transmitters and with a GSM power density level up to 60 µW/m².

The impact of indoor wireless devices such as DECT, Wi-Fi, and Bluetooth (the latter are not specifically mentioned in the graphs) are shown in Fig. 5. Within the first year after the activation of the GSM transmitter, i.e. until and including January 2005, the group with indoor wireless devices shows the strongest responses.
It is possible that in the less exposed subjects seasonal fluctuations or other factors such as "overshooting" of the values could have played a role. It should be noted here that both the average as well as the median adrenaline values increased after the activation of the transmitter and decreased again after one year. This, however, only applies to exposure levels >60 µW/m². Chronically ill subjects and children showed especially strong responses; except for some "outliers," no effect was observed in healthy adults.

The adrenaline level of overweight subjects and those with an amalgam burden hardly changed during the study period (Fig. 6). In contrast, chronically ill subjects showed especially strong responses above average. In fact, the increase in the median values between January and July 2004 for all study subjects was predominantly caused by children and chronically ill subjects; adults without any chronic disease show a flat curve. During this period, an increased adrenaline level between 5 and 10.3 was measured in three healthy adults. Because of these "outliers," the average values for healthy adults clearly increased in contrast to the median values.

![Fig. 6: Median adrenaline levels for participating children, for chronically ill subjects, for those with amalgam burden, and overweight subjects in Rimbach in comparison to the median levels of all study subjects and adults without chronic disease](image)

The lower sensitivity of subjects with an amalgam burden can be explained by the fact that the effect occurs more often in children and that children according to our definition are younger than 10 years. They have hardly any fillings with amalgam.

### Noradrenaline

The results for noradrenaline are similar to those for adrenaline (Tab. 4, Fig. 7). The statement that individual noradrenaline levels from January to July 2004 increased is statistically well supported with p<0.001. The fact that the levels dropped between July 2004 and July 2005 is also well supported with p<0.0005. Like in the case of adrenaline, the period under investigation is July 2004 to July 2005 to take the delayed decrease in the high exposure group into consideration. According to Table 4, the median of all noradrenaline levels increased from January to July 2004 for 11.2 µg/g creatinine; for exposures up to 60 µW/m², there were 2.2 µg/g creatinine, at 60-100 µW/m² 12.4 µg/g creatinine, and above 100 µW/m² 12.3 µg/g creatinine. As in the case of adrenaline, the increase for the last two groups is almost the same. Again, it is not possible to statistically verify a dose-response relationship. In Figure 7, a dose-response relationship

Tab. 4: Results for the noradrenaline levels in µg/g creatinine

<table>
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<td>Median</td>
<td>Average</td>
<td>Median</td>
</tr>
<tr>
<td></td>
<td>55.8</td>
<td>49.8</td>
<td>57.7</td>
<td>53.5</td>
</tr>
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<td>Average</td>
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<td>44.3-59.1</td>
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<tr>
<td>µW/m²</td>
<td>CI</td>
<td>Average</td>
<td>Median</td>
<td>35.1-67.8</td>
</tr>
<tr>
<td>60-100</td>
<td>CI</td>
<td>Average</td>
<td>Median</td>
<td>38.0-59.1</td>
</tr>
<tr>
<td>µW/m²</td>
<td>CI</td>
<td>Average</td>
<td>Median</td>
<td>49.9-87.3</td>
</tr>
</tbody>
</table>

Fig. 7: Median noradrenaline levels in all participating citizens of Rimbach as a function of GSM power density levels (peak values)

Fig. 8: Median noradrenaline values for subjects who had a DECT phone or other wireless devices at home, for those without indoor wireless devices, as well as for subjects without indoor wireless devices and with a GSM radiation exposure up to 60 µW/m² (peak value measured in front of residence)
is seen, whereby the dot-dashed line serves as reference for persons with very low exposures. It stands out that the “recovery period,” i.e. the decrease in values in 2005, drags on for longer in subjects in the exposure group with GSM radiation levels above 100 µW/m². This also corresponds with the behavior of the adrenaline levels.

In comparison with adrenaline, noradrenaline plays a somewhat greater role in residences where wireless devices existed before the beginning of this study (Fig. 8).

The trend in Figure 9 shows that children and chronically ill subjects in contrast to overweight subjects express strong responses to cell tower radiation. The ratios, however, are not as clearly visible as with adrenaline. Especially in overweight subjects, they indicate a slow response to GSM radiation.

Noradrenaline and adrenaline, however, responded very similarly.

4 Dopamine

For dopamine, inverse effects to those for adrenaline and noradrenaline were observed. The median dopamine levels decreased from 199 to 115 µg/g creatinine between January and July 2004 (Tab. 5). The fact that the dopamine levels of the study subjects decreased during this period is highly significant (p<0.0002). Thereafter, the median increased again: In January 2005, it was at 131 µg/g creatinine, in July of this year 156. This increase is also significant (for increase between July 2004 and July 2005 p<0.05).

This, too, is a dose-response relationship: from January to July 2004, the median for all subjects decreased for 84 µg/g creatinine, in the exposure group up to 60 µW/m² for 81, in the exposure group above 100 µW/m² even 153 µg/g (see Tab. 5 and Fig. 10). This dose-response relationship is statistically significant based on the signed-rank Wilcoxon test (12) with p<0.025. The following statement applies: “The decrease in dopamine levels for exposure levels up to 100 µW/m² is smaller than at exposure levels above 125 µW/m².”

In subsequent laboratory tests, the dopamine levels do not return to the same level as in January 2004. From Figure 11, it is obvious that the correlation with prior exposures to indoor wireless devices is small.

### Tab. 5: Results for dopamine levels in µg/g creatinine

<table>
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<tbody>
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<td>158</td>
<td>138</td>
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<tr>
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<td>115</td>
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<td></td>
<td>CI</td>
<td>168-273</td>
<td>86-160</td>
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</tr>
<tr>
<td>0-60 µW/m²</td>
<td>Average</td>
<td>217</td>
<td>183</td>
<td>139</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>189</td>
<td>108</td>
<td>116</td>
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<tr>
<td></td>
<td>CI</td>
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<td>80-254</td>
<td>90-157</td>
</tr>
<tr>
<td>60-100 µW/m²</td>
<td>Average</td>
<td>242</td>
<td>161</td>
<td>140</td>
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<tr>
<td></td>
<td>Median</td>
<td>223</td>
<td>150</td>
<td>131</td>
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<tr>
<td></td>
<td>CI</td>
<td>137-335</td>
<td>94-168</td>
<td>93-164</td>
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<tr>
<td>&gt;100 µW/m²</td>
<td>Average</td>
<td>244</td>
<td>115</td>
<td>147</td>
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<tr>
<td></td>
<td>Median</td>
<td>244</td>
<td>91</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>CI</td>
<td>139-316</td>
<td>48-202</td>
<td>117-169</td>
</tr>
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</table>

CI = 95% confidence interval of median

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It is to be emphasized that the lowest exposure group without such indoor wireless devices and with a GSM power density level < 60 µW/m² responds almost as strongly as all other study subjects. This is consistent with the data in Figure 10: the data suggest that the effect of the radiation on the dopamine levels can already be observed at very low power density levels; however, it still can increase at levels above 100 µW/m².

Figure 12 shows that the radiation effect is somewhat more pronounced in children compared to the average, i.e. the gradient of the curves between the first two data points is somewhat greater. However, the difference is far too small to be statistically significant.

In summary, dopamine levels decreased after the activation of the GSM transmitter and were not restored to the initial level over the following one and a half years. A significant dose-response relationship is observed. In children, the decrease is somewhat more pronounced than in adults.

5 Phenylethylamine (PEA)

Phenylethylamine (PEA) levels respond more slowly to the radiation compared to the substances investigated so far (Tab. 6, Fig. 13). Only in the exposure group above 100 µW/m² GSM radiation do the PEA levels decrease within the first six months. Thereafter, hardly any differences can be discerned between PEA values of the various power density levels investigated here.

The decrease of PEA levels between July 2004 and July 2005 is highly significant (p<0.0001)

Similar to adrenaline and noradrenaline, a previous exposure to indoor wireless devices intensifies the effect of the GSM radiation (see Fig. 14). The subjects of the low-exposure groups without indoor wireless devices do respond in a time-delayed fashion, but after six months they respond just as clearly as the subjects of the highest exposure group. In this regard, the PEA levels behave like those of dopamine in contrast to adrenaline and noradrenaline, which only respond to stronger fields.
In children, the effect of GSM radiation on their PEA levels is no greater than in the average of the study subjects; healthy adults do not respond substantially differently. In contrast to the other substances looked at so far, the group of overweight subjects does respond particularly rapidly to PEA.


discussion

Catecholamine System and Phenylethylamine (PEA)

The survival of mammals depends on their ability to respond to external sources of stress. An established, well-researched axis of the human stress system represents the catecholamine system (6, 15, 16). It can be activated by psychic or physical stressors. Impulses mediated by nerves are responsible for an induction of the catecholamine biosynthesis at the level of tyrosine hydroxylase as well as dopamine beta-hydroxylase, whereby the effect is based on an induction of both enzymes. Many biochemical regulatory mechanisms tightly control catecholamine synthesis (8, 15, 17). Chronic dysregulation always leads to health problems in the long run. The development of high blood pressure under continuous stress serves as a clinical example; so-called "beta blockers" directly block the action of adrenaline and noradrenaline on the target receptors, and it is impossible to imagine medication-based therapy without them (15).

PEA can be synthesized from the essential amino acid phenylalanine either via tyrosine, dopamine, noradrenaline, and adrenaline or via a direct biochemical path (15) (Fig. 16). The sympathetic-mimetic effect of PEA was first described by Barger in 1910 (18).

PEA is also synthesized from phenylalanine and is considered a superordinate neuromodulator for the regulation of catecholamine synthesis (19-22).
In 1976, Zeller described the physiological relationships (23) and points out that PEA is released by the brain via electrical stimulation (24).

The effect mechanism of PEA in the catecholamine system is the center of current pharmaceutical research efforts. In molecular biological terms, intracellular TAAR (trace amine-associated receptor) G-protein-coupled receptors that mediate modulatory effects of PEA are verified (20).

For high nanomolar to micromolar PEA concentrations, in vivo studies have shown amphetamine-like effects. During an increase of PEA, an increased amount of noradrenaline and dopamine is also released and the reuptake of these substances is impaired (25, 26).

According to Burchett, the following effects of PEA amplifying the catecholamine effect are assumed to be known: Direct agonist action via increased release of transmitters, reuptake inhibition, and stimulation of transmitter synthesis as well as inhibition of monamine oxidase (MAO) (19). PEA’s high lipophilicity—a prerequisite for the permeability of membrane barriers such as the blood–brain barrier—is of note here; PEA levels in the brain, serum, and urine correlate quite well (10, 21, 25, 27).

The clinical relevance of changed PEA levels is well documented for mental illnesses. Endogenous depression is associated with lowered PEA levels, whereby the transition from depression to manic episodes is accompanied by an increase in PEA levels (28-32).

The therapeutic increase in the PEA level has a positive impact on the course of the disease. Phenylalanine improves the effectiveness of antidepressants; PEA by itself is a good antidepressant—effective in 60% of the cases of depression.

In persons with ADD/ADHD (attention deficit hyperactivity disorder), PEA levels are substantially lower; the ADHD treatment with methylphenidate (Ritalin®) normalizes PEA excretion in the urine of responders (33, 34).

**Contributing Factors**

Laboratory tests of catecholamine have been established for years. Increased values are found in disorders such as pheochromocytoma, neuroblastoma, and arterial hypertension, whereby it is possible for a subject to consciously regulate these values. Especially urine tests offer a sufficient level of sensitivity and specificity because urine contains 100 to 1000 times higher levels than blood plasma. The intraindividual variation coefficient ranges from 7% to 12% from one day to another; stored under appropriate conditions, the stability of the samples can be guaranteed without problems (8).

In Rimbach, urine samples were always collected at the same time of the day so that a circadian dependence could be ruled out. Other contributing factors such as increased physical activity as well as large meals were also ruled out by collecting the urine in the morning. Seasonal factors of the samples collected twice in winter and summer should have been reflected as undulating levels in the testing results. Only in the adrenaline levels of the lower exposure groups (Fig. 5) can such a corresponding correlation be found. All other data did not indicate any seasonal influences.

In the study presented here, the selection of the participating citizens of Rimbach was not based on random assignment, but on self-selection. We can assume that the subjects, especially the adults, had informed themselves about the issue of cell tower radiation. However, because it is impossible to consciously regulate these levels, this self-selection should not make any difference in this study.

Especially in children below age ten, it is not thought possible to maintain a chronic state of anxiety for one and a half years due to an abstract term such as cell tower radiation.

This study limits itself to the following type of questions: “Did the level of a given substance predominantly increase or decrease during the study period?” Independent of each model, this question can be clearly answered with the Wilcoxon test and the indication of the confidence interval. The corresponding results are statistically very well supported. Any statements beyond this e.g. the dependence of levels on certain parameters—cannot be made because with 60 study subjects the number of cases is too small to establish the same type of statistical significance.

The great advantage of the “Rimbach data” is that prior to January 2004 the exposure levels were very low because there was no cell phone tower and because only a few citizens had installed DECT, Wi-Fi and similar devices. In addition, due to the testing equipment with a measurement accuracy of less than ± 3 dB combined with repeated control measurements, the classification of the exposure groups can be considered to be verified.

For the stress hormones adrenaline and noradrenaline, the increase occurred only after the installation and activation of the transmitter, and thereafter, levels continued to decrease but did not fully normalize.

For dopamine, significant differences in the dose-response relationship according to exposure group could be shown after the activation of the new cell tower antenna. Also, the consistently decreasing levels of the hypothetically superordinate regulatory PEA do not support the hypothesis that the stress factor for the observed changes in the adrenergic system would exclusively be found in the realm of psychological factors.

**Mode of Action of Microwave Radiation**

There is a wide range of evidence to interpret the newly emerging microwave exposures as an invisible stressor.

Microwaves are absorbed by living tissue. The frequencies used for cell phone technologies have a half-life penetration depth of several centimeters, whereby cell membranes constitute no obstacle (35).

Microwaves cause enzymes to malfunction directly by, for example, monomerization (36). Thus, it is conceivable that enzymes of the catecholamine system could be affected directly.
Intracellular processes are changed, and cellular mitosis is disturbed by forces acting on the cellular spindle apparatus (37, 38). The human body is required to provide a higher level of repair services that is comparable to a chronic state of stress. A decrease in adenosine triphosphate (ATP) due to microwave exposure could be demonstrated by Sanders in intracerebral tissue already in 1980 (39).

Within current exposure limits, Friedman could show the stress caused by microwaves in the cell membranes of a cell model (40). The oxygen radicals formed by NADH have an activating effect on subsequent intracellular cascades that amplify the membrane effect by a factor of $10^7$, which in turn substantially change intracellular processes (17). Even reproductive impairments due to microwaves are mediated by the formation of free radicals (41).

In industry, more and more microwave devices are being used for chemical peptoid syntheses, which allow for a 100 times faster and more precise production even without any measurable heating (42). The toxic effects of free radicals formed by microwaves are used in such technical applications as water purification (43).

In several studies, the chronic symptoms of residents near cell tower antennas were described (44-48). Interestingly, the expansion of wireless networks corresponds with the increase in prescription expenses for methylphenidate, a drug whose chemical structure is related to PEA and which is indicated in cases of attention deficit disorder (ADD) (49).

Long-term studies over five years suggested an increased cancer incidence due to microwave exposure (50, 51). Since the catecholamine system is directly linked with the nervous system within the psychoneuroimmunological framework beside its organ-specific effects, the observed increase in cancer incidence can now also be understood from a pathophysiological perspective (6, 15, 52, 53).

Hypothesis of the Course of the Stress Response in Rimbach

Significant research on the stress-response axis was carried out in the 1950s. Selye established the nowadays generally accepted theory of the general adaptation syndrome of the human body to a stressor (16). He distinguished between three stages in the stress response, which can be found again in the description of the microwave syndrome according to Hecht (2, 3). Thus, after the stages of alarm and resistance, the last stage of exhaustion sets in (Fig. 17). The parameters investigated in the Rimbach study follow this pattern.

STAGE I—Activation Stage

The results of the long-term study presented here show an immediate activation of the adrenergic system. After the activation of the cell phone base station under investigation, the parameters adrenaline and noradrenaline increase significantly within a period of one and a half years. Because of the increased production of the final hormones noradrenaline/adrenaline, the use of dopamine increases, and as a result, the dopamine level decreases. The decrease in the dopamine level is the more pronounced, the higher the GSM radiation exposure level is at the residence of the individual participants.

STAGE II—Adaptation Stage

After this sympathicotonic activation stage, the body tries to compensate the increase in adrenaline and noradrenaline. In order to inhibit the overshooting catecholamine production and to ensure a stable regulation, the phenylethylamine level (PEA level) decreases. Here the decrease in PEA starts in the highest exposure group first.

STAGE III—Premorbid Stage

According to our hypothesis, the effects of adrenaline and noradrenaline are inhibited by feedback mechanisms at the expense of a chronically, over six continuous months, lowered PEA level. However, the attempt at counterregulation remains incomplete—even one and a half years after the installation of the cell phone base station; the hormonal balance had not been restored completely. The PEA level remains at a low level, which is to be interpreted as evidence for the beginning of exhaustion.
Conclusion

Thus, the following hypothesis is proposed: Although participants maintained their usual lifestyle, they developed chronic stress with a primary increase in adrenaline/noradrenaline and a subsequent decrease in dopamine in response to the microwave exposure from the newly installed cell phone base station. During the stage of counterregulation, the "trace amine" PEA decreases and remains decreased.

This is of considerable clinical relevance because psychiatric symptoms also exhibit altered PEA levels. In Rimbach, the increase in sleep problems, cephalgia, vertigo, concentration problems, and allergies could be clinically documented after the cell phone base station had been activated. The newly developed symptoms can be explained clinically with the help of disturbances in the humoral stress axis (53).

After having exhausted the biological feedback mechanisms, major health problems are to be expected. The possible long-term consequences of remaining caught in the exhaustion stage have already been described by Hecht and Selye (3, 16).

Thus, the significant results presented here not only provide clear evidence for health-relevant effects in the study subjects of Rimbach after a new GSM base station had been installed there, but they also offer the opportunity to carry out a causal analysis. This has already been successfully done in the "shut-down study" of Schwarzenburg, Switzerland (54). In Rimbach, the documented levels should return to normal once the relevant base station is shut down.

Epidemiological Evidence

There is current epidemiological evidence for the considerable clinical relevance of the dysfunction of the humoral stress axis with its endpoints of PEA decrease and adrenaline increase, as documented by us.

1. Decreased PEA levels can be found in a large portion of ADD/ADHD patients. As therapy methylphenidate is used, a substance that is structurally related to PEA. Between 1990 and 2004, the boom time of cell phones, prescription costs for this medication had increased by a factor of 86 (49, 55).

2. As part of the German Mobile Telecommunication Research Programme, approximately 3000 children and adolescents were studied in Bavaria for their individual cell phone radiation exposure levels in relation to health problems. Among the various data sets, the data set regarding behavioral problems showed a significant increased risk for both adolescents (OR: 3.7, 95%-CI: 1.6-8.4) and also children (OR: 2.9, 95%-CI: 1.4-5.9) in the highest exposure group (56). For the first time, the "Rimbach Study" provides a model of explanation in biochemical terms.

3. Pheochromocytoma are adrenaline- and noradrenaline-secreting tumors of the adrenal gland (57). This type of tumor due to microwave exposure has already been demonstrated in animal experiments in 1985 (5). The increase of this disease in the US population is highly significant. Concurrent with the increase in local microwave exposures due to an increased number of base stations and use of wireless communication technologies, the number of cases have increased from 1,927 to 3,344 between 1997 and 2006 (58, 59).

It is a physician’s responsibility—not bound by directives—to work toward the preservation of the natural basis of life regarding human health (60). Now it is the duty of the responsible agencies (public health department, Bavarian State Ministry of the Environment and Public Health as well as other federal ministries) to investigate the current situation.

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