Comparison of the body fluid levels in healthy individuals and those with schizophrenia in Japan: Using the bioelectrical impedance method

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Abstract Polydipsia and water intoxication have been found to be care problems in people with schizophrenia in many countries. This Japanese study measured the body fluid distribution and body fat of 80 males with long standing schizophrenia and compared this to that of 64 healthy males, using bioelectrical impedance spectrum analysis (BIS). Participants with schizophrenia exhibited significantly lower percentages of intracellular fluid and total body fluid, and significantly higher percentages of fat. Moreover, the percentage of extracellular fluid was distributed over a wider range. When the percentage body fluid was compared between the two groups by matching body mass index and body fat, intracellular fluid was significantly lower for those participants with schizophrenia. There findings suggest that nurses and other health professionals need to be very cautious when attempting to modify the excessive drinking of fluids by patients with schizophrenia. In mistakenly trying to prevent water intoxication, they may in fact be contributing to dehydration.

Key words bioelectrical impedance, body fluid level, polydipsia, schizophrenia, water intoxication.

INTRODUCTION
Over a number of decades, there have been reports of polydipsia and water intoxication in psychiatric patients (Barahal, 1938; Rosenbaum et al., 1979; Singh et al., 1985; Bremner & Regan, 1991; Vishwajeet & Aneesh, 2005) and, in 1993, Hoskins et al. (1993) reported that patients with schizophrenia exhibited an elevated urinary output. In Europe and the USA, polydipsia is seen in 20–29% of psychiatric patients, while water intoxication is detected in ≈ 5% of these patients (de Leon et al., 1994; de Leon, 2003; Costanzo et al., 2004). In Japan, Matsuda (1988) reported the incidence of polydipsia and water intoxication in psychiatric inpatients at 10.8% and 3.3%, respectively, and related factors noted have included the syndrome of the inappropriate secretion of antidiuretic hormone (SIADH) as an adverse reaction to a psychotropic agent and the use of anticholinergics. However, although long-term institutionalization for mental disorders, smoking, and interpersonal relationships have been implicated, no conclusive causation has been obtained for polydipsia and water intoxication (Allon et al., 1990; Amagai, 1995; Siegler et al., 1995; de Leon et al., 1996; Michael & Shutty, 1996; de Leon et al., 2002; Miyamoto et al., 2002; Kishimoto & Hirayama, 2004).

Polydipsia can lead to various severe symptoms. For example, the patient might have behaviors that cause many disturbances within psychiatric nursing settings or have convulsions that lead to possible death (Nakayama et al., 1995). Therefore, it is important to identify patients who drink excessive quantities of water so that early detection and prevention of this behavior is eliminated (Enokida & Yamauchi, 1992). In order to detect water intoxication early, it is necessary to objectively assess the volume of body fluid, observe patient behaviors, and ascertain the level of risk. In the past in Japan, the body weight was measured at regular or irregular intervals or blood tests were conducted to measure the levels of electrolytes and the hematocrit (Sakamoto, 1992). Although several studies have analyzed the relationship of polydipsia to body weight, urine volume or specific gravity, the threshold for an increased risk of ill health has not been clarified. At present, the average patient length of stay in psychiatric hospitals in Japan is ≈ 360 days; however, the participants in this study had been in hospital for a significantly longer period. Inpatients have often received behavioral
restrictions that become a source of stress for them and that might contribute to them increasing their water intake. Some reports indicated that excessive water-drinking behaviors of patients stopped when their behavioral restrictions were abolished (Yamauchi, 2002; Takahashi & Sakutori, 2003; Yoshihama et al., 2003).

Aim
The aim of this study was to ascertain the distribution of body fluid among male patients with schizophrenia and to compare this with body fluid distribution among healthy individuals using bioelectrical impedance spectrum (BIS) analysis.

Bioelectrical impedance spectrum analysis
This is a simple, uninvasive technique to measure body fluid using a small, alternating current of 5 kHz to 1 MHz. Using a four electrode method, the BIS is measured between the right wrist and right ankle (Nakadomo et al., 1991; Maruyama & Kondo, 1992). Electrical resistance or impedance is measured to estimate body composition, allowing various body fluid levels to be measured easily and uninvasively. The validity and reliability of BIS was confirmed some years ago (Kushner & Schoeller, 1986; Nakadomo et al., 1990). In some clinical settings other than mental health, the BIS has been used for fluid management and nutritional assessment in relation to dialysis, chemotherapy related to cancer, and in relation to AIDS (Maruyama, 1993; Ludy et al., 2005; Schols et al., 2005; Gul et al., 2006).

METHODS
Participants
The participants were 80 men aged 31–59 years who were diagnosed with schizophrenia according to the DSM-IV, which was in use in Japan during the study (American Psychiatric Association, 1995). They were inpatients at five psychiatric hospitals in one prefecture in Japan. The following patients were excluded from the present study: those taking carbamazepine or lithium, as these drugs can affect the body fluid (de Leon et al., 1996; Sudoh et al., 2001); those taking diuretics; and those being treated for diabetes. All the participants took antipsychotic medications, including typical long-standing drugs such as haloperidol or chlorpromazine or more recent atypical drugs, such as olanzapine or risperidone.

The control group consisted of 64 men aged 31–59 years who had undertaken screening to determine that they were healthy. These men were recruited at random from a private medical clinic that they attended for the purpose of a general employment health check-up. The physicians and manager of the clinic agreed to the study. Prior to their check-up, an explanation of the study was given orally and in writing to the men and consent was obtained to view the results of their health check with the physician. Each man had the same health check and a common medical form was used. After the check-up, if there were no problems with their health status, they were recruited to the study.

Ethical considerations
The study protocol was approved by the Yamaguchi University Ethical Review Board and the Yamaguchi University Medical School and Hospital Bioethics Committee. Furthermore, the study was conducted with approval from the administrator of each of the five participating institutions. Explanations of the research were given in writing and orally to the potential participants. Where the participants were unable to give informed consent for involvement in the study because of their mental condition, consent was obtained from their doctor and their next-of-kin. Consent to review the medical charts and to collect information from physicians and hospital staff was also obtained.

For participants in the control group, the details of the study were explained orally and in writing on the day of the health screening to obtain consent for the BIS measurement. Consent to review the results of their health screening was obtained at the same time. It was clearly stated to all participants that participation was voluntary and that consent could be withdrawn at any time, even in those cases where a doctor or the next-of-kin gave consent on behalf of a patient. It was explained that refusal to participate would not result in any negative consequence and privacy would be protected throughout the study.

Data collection
The data were collected during the spring of two consecutive years to avoid influences from the climate. Basic patient data were obtained by reviewing medical charts and interviewing physicians and nurses. The BIS was measured before lunch at 10.00–11.00 hours when, according to the opinion of the medical staff, patients were considered to be more psychologically stable. Before each measurement, the participants were asked to provide a urine sample for the measurement of specific gravity. As a general rule, the BIS was measured on three consecutive days, and the averages were used. When the BIS could not be measured on three days due to the mental or physical status of the participants, the averages were calculated from the available data. Although there were no particular restrictions on drinking or eating on the day of the BIS measurement, the participants were instructed to avoid vigorous exercise for 1 h before the measurement.

Before the measurement, the participants were asked to empty their bladder and bowel and to remove their jewelry and socks. They were then asked to lie on the bed in the supine position and spread their arms away from their body and they were positioned so that their legs were opened 30° (Fig. 1). The four electrodes for the BIS machine were positioned after wiping the skin with 50% isopropyl alcohol and the measurements were commenced 1–3 min after attaching...
the electrodes. The participants were instructed to relax and try to stay calm during the measurement.

**Data analysis**

SPSS 11.0J (SPSS Japan, Tokyo, Japan) was used for the data analysis. From the fat-free mass, the fat mass (FAT) was calculated. In order to compare the FAT, the ratios of total body fluid (TBF), intracellular fluid (ICF), and extracellular fluid (ECF) to body weight were calculated (%FAT, %TBF, %ICF and %ECF, respectively). In the present study, a complex bioimpedance spectrum analysis system (400C; XITRON Technologies, San Diego, CA, USA), equipped with IS4000 electrodes, was used to measure the BIS.

**RESULTS**

Table 1 shows the basic data and the various body fluid levels for the participants in the control and schizophrenia groups. The average age among the schizophrenia group was 49.4 ± 7.8 years and the average disease duration was 25.8 ± 10.3 years, ranging from 2–42 years. The average dose of antipsychotic agent (as chlorpromazine) was 902.4 ± 776.1 mg. The average age among the control group was 47.5 ± 5.8 years.

When the height, body weight, and Body Mass Index (BMI) were compared by t-test between the two groups, no significant differences were detected; hence, the two groups were considered to have similar body shapes. In terms of the percentage body fluid and %FAT, no significant intergroup difference was apparent for the %ECF. However, in the schizophrenia group, the %ICF and %TBF were significantly lower and the %FAT was significantly higher ($P < 0.01$) (see Table 2 and Fig. 2).

Figure 3 shows the distribution of percentage body fluid for the schizophrenia group and the healthy individuals. None of the control group exhibited a %ICF < 25% or a %ECF < 21%. In contrast, in the schizophrenia group, the %ICF was < 25% in seven participants and the %ECF was < 21% in two participants. Moreover, when compared to the control group, the %ICF for the schizophrenia group was generally lower, while the %ECF for the schizophrenia group was distributed over a wider range (Fig. 3).

As the %FAT influences the body fluid levels, the various body fluid level percentages were compared between the two groups by matching the BMI and %FAT (see Table 3). Although no significant differences were observed for the %TBF or %ECF, the %ICF was significantly lower in the schizophrenia group (32.32%) than in the control group (33.46%) ($P < 0.05$).

**DISCUSSION**

**Comparison of body fluid between the two groups**

In general, the body fluid percentage is ≈ 60% in Japanese adults (Iino, 2002). In the present study, although the %TBF for the healthy individuals was 60.48%, that of the participants with schizophrenia was significantly lower, at 58.86%.
In our previous study on female patients with schizophrenia (Satoh et al., 2002), the %TBF was significantly lower in women with schizophrenia (50.33%) than in healthy women (56.65%). Furthermore, in the present study, the %ICF for the male subjects with schizophrenia was significantly lower than that for healthy men, in accordance with our previous findings for females.

Although thirst and polydipsia in psychiatric patients are believed to be caused by such factors as psychotropic agents, SIADH, and smoking (Allon et al., 1990; Amagai, 1995; Siegler et al., 1995; de Leon et al., 1996; Michael & Shutty, 1996; Miyamoto et al., 2002), there are no substantiated findings on this issue. However, the results of our previous and present studies suggest that the percentage body fluid of individuals with schizophrenia is lower than that of healthy individuals and this could therefore be one of the causes of thirst.

As far as the cause of relative dehydration is concerned, although body shape and the BMI were comparable between the two groups, the %FAT was significantly higher among the participants with schizophrenia. As adipose tissue does not contain a high amount of water, a high percentage of body fat equates to a low percentage of body fluid for a given body weight. Conversely, a low %FAT tends to be associated with high muscle mass, which has high water content. In long-term psychiatric patients in Japan, polydipsia, water intoxication, obesity, and lifestyle-related diseases are problematic. The latter two are believed to be high because of a chronic lack of exercise and the use of antipsychotic drugs (Nagamine, 2001). Nonetheless, as the muscle mass of psychiatric inpatients tends to be low, it is not possible to ascertain from body fluid percentage alone whether the high %FAT is due to an increase in %FAT itself or a decrease in muscle mass.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients with schizophrenia</th>
<th>Healthy individuals</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>80</td>
<td>64</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49.4 ± 7.8</td>
<td>47.5 ± 5.8</td>
<td>–1.66</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.2 ± 5.2</td>
<td>167.6 ± 5.2</td>
<td>1.73</td>
<td>NS</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>65.1 ± 9.6</td>
<td>66.0 ± 8.8</td>
<td>0.55</td>
<td>NS</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>23.2 ± 3.2</td>
<td>23.0 ± 2.6</td>
<td>–0.35</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.

**Table 2. Percentage body fluid of patients with schizophrenia and healthy individuals**

<table>
<thead>
<tr>
<th>Body fluid</th>
<th>Patients with schizophrenia</th>
<th>Healthy individuals</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>80</td>
<td>64</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>%ECF</td>
<td>25.54 ± 2.92</td>
<td>25.32 ± 1.83</td>
<td>–0.52</td>
<td>NS</td>
</tr>
<tr>
<td>%ICF</td>
<td>30.27 ± 3.85</td>
<td>35.15 ± 3.77</td>
<td>7.65</td>
<td>**</td>
</tr>
<tr>
<td>%TBF</td>
<td>55.86 ± 5.94</td>
<td>60.48 ± 4.92</td>
<td>5.11</td>
<td>**</td>
</tr>
<tr>
<td>%FAT</td>
<td>25.75 ± 7.71</td>
<td>18.78 ± 6.47</td>
<td>–5.90</td>
<td>**</td>
</tr>
<tr>
<td>I/E ratio</td>
<td>1.19 ± 0.16</td>
<td>1.39 ± 0.13</td>
<td>7.93</td>
<td>**</td>
</tr>
</tbody>
</table>

**P < 0.01. ECF, extracellular fluid; FAT, fat mass; ICF, intracellular fluid; I/E, intracellular to extracellular fluid ratio; NS, not significant; TBF, total body fluid.**

**Figure 2.** Comparison of the percentage body fluid between patients with schizophrenia and healthy individuals. **P < 0.01. (■) Schizophrenia group; (□) control group. ECF, extracellular fluid; FAT, fat mass; ICF, intracellular fluid.**

In our previous study on female patients with schizophrenia (Satoh et al., 2002), the %TBF was significantly lower in women with schizophrenia (50.33%) than in healthy women (56.65%). Furthermore, in the present study, the %ICF for the male subjects with schizophrenia was significantly lower than that for healthy men, in accordance with our previous findings for females.

Although thirst and polydipsia in psychiatric patients are believed to be caused by such factors as psychotropic agents, SIADH, and smoking (Allon et al., 1990; Amagai, 1995; Siegler et al., 1995; de Leon et al., 1996; Michael & Shutty, 1996; Miyamoto et al., 2002), there are no substantiated findings on this issue. However, the results of our previous and present studies suggest that the percentage body fluid of individuals with schizophrenia is lower than that of healthy individuals and this could therefore be one of the causes of thirst.

As far as the cause of relative dehydration is concerned, although body shape and the BMI were comparable between the two groups, the %FAT was significantly higher among the participants with schizophrenia. As adipose tissue does not contain a high amount of water, a high percentage of body fat equates to a low percentage of body fluid for a given body weight. Conversely, a low %FAT tends to be associated with high muscle mass, which has high water content. In long-term psychiatric patients in Japan, polydipsia, water intoxication, obesity, and lifestyle-related diseases are problematic. The latter two are believed to be high because of a chronic lack of exercise and the use of antipsychotic drugs (Nagamine, 2001). Nonetheless, as the muscle mass of psychiatric inpatients tends to be low, it is not possible to ascertain from body fluid percentage alone whether the high %FAT is due to an increase in %FAT itself or a decrease in muscle mass.

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In terms of lifestyle factors, the average duration of schizophrenia in the participants was 25 years and this would have had a significant but unmeasured effect on factors such as diet, exercise, work patterns, environment, and other activities of daily living. Furthermore, these participants had been institutionalized for \( \approx 10 \) years on average, and few had been hospitalized for \(< 1 \) year. The study participants had therefore been taking antipsychotic drugs for a long period of time, some for \( \approx 25 \) years. Some of the adverse reactions associated with antipsychotic drugs include extrapyramidal disorders, such as parkinsonism, dyskinesia, and akathisia (Toru, 2001). As a result of these reactions and of the disease itself, spontaneity and volition are reduced, leading to a lack of exercise. Even the participants who had experienced relatively brief hospitalization at the time of the study had been repeatedly admitted and had been administered antipsychotic drugs. Moreover, few of the participants had regular employment, another factor that is associated with reduced levels of physical activity. All of these factors could have resulted in reduced muscle mass among the participants, thus affecting their body fluid levels.

Table 3. Comparison between the schizophrenia and control groups when the Body Mass Index (BMI) and percentage fat mass (%FAT) were matched

<table>
<thead>
<tr>
<th>Body fluid</th>
<th>Patients with schizophrenia</th>
<th>Healthy individuals</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>22</td>
<td>34</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.8 ± 8.0</td>
<td>47.5 ± 6.0</td>
<td>0.69</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>23.2 ± 2.0</td>
<td>23.2 ± 2.1</td>
<td>0.18</td>
<td>NS</td>
</tr>
<tr>
<td>%ECF</td>
<td>25.59 ± 2.06</td>
<td>24.73 ± 1.11</td>
<td>1.96</td>
<td>NS</td>
</tr>
<tr>
<td>%ICF</td>
<td>32.32 ± 1.52</td>
<td>33.46 ± 1.88</td>
<td>-2.38</td>
<td>*</td>
</tr>
<tr>
<td>%TBF</td>
<td>57.87 ± 2.59</td>
<td>58.19 ± 2.02</td>
<td>-0.52</td>
<td>NS</td>
</tr>
<tr>
<td>%FAT</td>
<td>22.58 ± 3.23</td>
<td>21.75 ± 2.91</td>
<td>0.99</td>
<td>NS</td>
</tr>
<tr>
<td>I/E ratio</td>
<td>1.27 ± 0.12</td>
<td>1.36 ± 0.11</td>
<td>-2.81</td>
<td>**</td>
</tr>
</tbody>
</table>

\( *P < 0.05; **P < 0.01 \). ECF, extracellular fluid; ICF, intracellular fluid; I/E, intracellular to extracellular fluid ratio; NS, not significant; TBF, total body fluid.

In terms of lifestyle factors, the average duration of schizophrenia in the participants was 25 years and this would have had a significant but unmeasured effect on factors such as diet, exercise, work patterns, environment, and other activities of daily living. Furthermore, these participants had been institutionalized for \( \approx 10 \) years on average, and few had been hospitalized for \(< 1 \) year. The study participants had therefore been taking antipsychotic drugs for a long period of time, some for \( \approx 25 \) years. Some of the adverse reactions associated with antipsychotic drugs include extrapyramidal disorders, such as parkinsonism, dyskinesia, and akathisia (Toru, 2001). As a result of these reactions and of the disease itself, spontaneity and volition are reduced, leading to a lack of exercise. Even the participants who had experienced relatively brief hospitalization at the time of the study had been repeatedly admitted and had been administered antipsychotic drugs. Moreover, few of the participants had regular employment, another factor that is associated with reduced levels of physical activity. All of these factors could have resulted in reduced muscle mass among the participants, thus affecting their body fluid levels.

As to the effects of antipsychotic drugs on body composition, antipsychotic drugs can increase the %FAT by increasing the appetite through 5-HT2 and D2 receptor blockage, suppressing prolactin secretion through D2 receptor blockage, and interacting with cholinergic neurotransmitters.
fluid levels do not exceed the normal %ECF of 28% and the prevention of water intoxication, it is necessary to ensure that body phrenia was lower than that of the healthy group. In order to restrict water intake in patients complaining of thirst. This finding suggests that thirst in schizophrenia is very different from that in healthy individuals. This author found that avoiding salty snacks, reducing smoking or sucking on candies were mostly ineffective in alleviating the thirst of patients with schizophrenia and that although many patients also complained of hunger, thirst in patients with schizophrenia might have been related to the effect of the brain’s feeding and thirst centers.

**Comparison with matching percentage fat mass and Body Mass Index**

The %FAT is a factor that markedly affects the %ICF. As the healthy individuals and participants with schizophrenia in the present study had comparable body shapes, the low %ICF could have had a marked impact on the %FAT. Therefore, the two groups were compared by matching the BMI and %FAT. Although there were no significant differences in the %TBF or the %ECF, the %ICF was significantly lower in the schizophrenia group ($P < 0.05$). The low %ICF in the schizophrenia group therefore appeared to reflect a unique phenomenon that is unrelated to increased %FAT. When water is consumed orally, the ECF levels initially increase. In the participants with schizophrenia, although the level of ECF was high due to polydipsia, the level of ICF was low. As far as intracellular dehydration is concerned, this might have resulted from a chronically inadequate water intake, leading to a reduced TBF. Kimura (1993; 2004) reported that thirst in patients with schizophrenia is different from that in healthy individuals. This author found that avoiding salty snacks, reducing smoking or sucking on candies were mostly ineffective in alleviating the thirst of patients with schizophrenia and that although many patients also complained of hunger, thirst in patients with schizophrenia might have been related to the effect of the brain’s feeding and thirst centers.

**Limitations**

This study has several important limitations as it was confined to male inpatients with schizophrenia; outpatients and patients with other mental disorders were not included. In addition, the number of participants and participating institutions were low. A further important limitation is that the researchers did not measure the relationship between the duration of schizophrenia and the length of hospital stay and level of body water. This is an important consideration for future research. Another limitation is that this study did not consider the difference in body fluid levels or polydipsia in patients who took different kinds of antipsychotic medications. Future research should focus on this to determine if particular kinds of antipsychotic medications produce different body fluid levels or affect polydipsia in patients in different ways. Clearly, more research is required to determine the cause of polydipsia and water intoxication in individuals with schizophrenia and to determine better strategies for modifying behaviors for their better health. A future study is therefore planned to further investigate body fluid distribution by studying more psychiatric patients to improve data accuracy and reliability.

**CONCLUSION**

In the present study, the participants with schizophrenia tended to suffer from intracellular dehydration and this could be one of the factors promoting their thirst and polydipsia. Our findings were threefold: (i) the body fluid levels were significantly lower in the patients with schizophrenia compared to the healthy individuals, and the patients with schizophrenia tended to be dehydrated; (ii) the I/E ratio was significantly higher in the healthy individuals; and (iii) the participants with schizophrenia might have been suffering from intracellular dehydration.

These results suggest that thirst in the patients suffering from schizophrenia might be a physiological response related to low levels of ICF and, therefore, caution is warranted when nursing and medical staff, or indeed patients themselves,
attempt to limit fluid intake to prevent water intoxication as this might in fact be causing low body fluid levels. Nurses must ensure that they carefully observe patients for signs of polydipsia and inform the care team of the possible need to measure the body fluid levels as a behavior modification program to reduce water intake might harm patients by causing dehydration.

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