Sleep and behavioral research: overview on global trends and Brazilian contributions to this field

Sono e pesquisa comportamental: panorama sobre tendências mundiais e contribuição brasileira neste campo

Gabriel Natan Pires1,2, Monica Levy Andersen2, Sergio Tufik3

ABSTRACT
The relationship between sleep and behavioral changes is quite clear. There are many neuro-behavioral co-morbidities that are related to sleep. In line with the aims of translational science, pre-clinical research has been shown to have great value for psychiatric research in Brazil and worldwide, and this importance can be extended to sleep studies. Thus, the present article aimed to present a broad view of basic behavioral science, especially the research using animal models, and focused on the global research output on the subject of "sleep", study trends and the Brazilian contribution to the field. The presented data demonstrate the increasing importance of Brazilian research to the field of sleep research, the Brazilian contribution to the worldwide knowledge of this subject and the adequacy of this theme to knowledge formation in the country, which is growing both in volume and publication relevance.

Keywords: Sleep; Behavioral research; Brazil

RESUMO
A relação entre sono e alterações comportamentais é bastante clara. Diversas são as comorbidades neuro-comportamentais relacionadas ao sono. Do ponto de vista da ciência translacional, a pesquisa pré-clínica tem se mostrado de grande valia à pesquisa psiquiátrica, tanto brasileira como mundial, e essa importância é extensível a estudos sobre sono. Desse modo, o presente artigo visou apresentar um panorama sobre a ciência básica comportamental, especialmente a conduzida com animais de experimentação, sendo enfocadas a produção global sobre o tema "sono", as tendências de estudo e a participação brasileira nesse cenário. Os dados apresentados demonstram a crescente importância da pesquisa brasileira às pesquisas do sono, a participação do Brasil na produção mundial sobre o tema e a adequação desse campo de pesquisa à realidade de formação de conhecimento do país, que é ascendente tanto em volume quanto em relevância de publicações.

Descritores: Sono; Pesquisa comportamental; Brasil

INTRODUCTION
The relationship between sleep and behavioral disturbances is quite clear1,2. There are many neuro-behavioral co-morbidities related to sleep and associated factors such as sleep restriction and sleep-disordered breathing3,4. Thus, the importance of this subject to psychiatric research is evident5, and demonstrated by many recent reviews that discuss the relationship between sleep and psychiatric disorders, such as depression6, anxiety7 and mood disturbance8.

Basic science and translational research, defined as the process by which ideas and discoveries derived from basic science research, become applicable to the treatment and prevention of human diseases9, and have greatly contributed to psychiatric research in general10, especially to Brazilian psychiatric research11. This contribution reflects the specific study relevance to the accumulation of knowledge about various specific disorders and psychiatric conditions and tends to extend to basic behavioral research and its relationship with sleep.

Knowing the importance of researches regarding the relationship between psychiatric disorders and sleep and considering the efficient way in which basic research approaches this association, the present article aimed to present a general overview of the relationship between basic and behavioral research, in particular the research that uses animal models to study sleep. The focus is on the global production of research on this subject, study trends and the Brazilian contribution to the field.

RESEARCH METHODOLOGY
From information obtained through the Web of Knowledge database, an estimate of the worldwide production on sleep and various relevant behaviors to translational science was made. The following descriptors were used in this estimation: “sleep”, “behavior”, “animals”, “rat”, “rats”, “mouse”, “mice”, “anxiety”, “depression”, “mood”, “stress”, “sexual behavior”, “aggression”, “aggressive behavior”, “feeding behavior” and “maternal behavior”, combined using the boolean operators “AND” and “OR”. In addition, “country/territory” and “publication year” filters were employed for further analysis.
The evolution of the literature on sleep in general was analyzed in a descriptive manner, with a focus on basic science research and the behaviors listed above. For this analysis, the period between 1945 and 2010 was considered, since it corresponds to the years catalogued in the employed database. Independent analyses were then performed for each considered behavior.

RESEARCH ABOUT SLEEP: A GENERAL ANALYSIS

Descriptor: “Sleep”
In the used database, a search for “sleep” found 89,194 publications. This list of publications exhibits a clear temporal influence, with an obvious increase in the number of publications year by year. As an example of this trend, the number of indexed publications from 1950 (18 publications), 1970 (416), 1990 (903) and 2009 (6,929) can be analyzed. In fact, during the 1990s, there was a large increase in the annual number of publications about sleep, a trend that has been maintained ever since. For example, the number of publications in 2009 represents a 113% increase compared to the number in 2000 and a 667% increase when compared to 1990.

The Brazilian production of sleep research publications follows the global trend toward increased productivity. Although it only entered the international publishing scene for this field in the 1980s (when it occupied the 20th position in publication numbers), Brazil currently offers unique contributions to worldwide publication on the subject; it is the 13th most prolific country in terms of sleep publications, with a total of 1,405 publications, corresponding to 1.57% of the total worldwide production. The last decade has shown an intense growth for Brazilian sleep research, as evidenced by the 567% increase in publication numbers between 2000 and 2009. When only 2009 is considered, Brazil ranks 9th in sleep publication and is responsible for 3.28% of the worldwide production. The Brazilian productivity in this field can also be seen when examining the institutions that produce the most publications on this subject. In 2009, Universidade Federal de São Paulo ranked 4th in the number of worldwide sleep publications, having published 98 articles. The top spots in this ranking were Harvard University (211 articles), The University of Pennsylvania (137 articles) and The University of Pittsburgh (104 articles).

SLEEP AND BASIC RESEARCH: GENERAL ANALYSIS

Descriptors: “Sleep” AND (“animals” OR “rat” OR “rats” OR “mice” OR “mouse”)
Similarly to general sleep research, the production of basic science papers on the subject also shows increases over time, although in a smaller proportion. Among the 89,194 studies on sleep that are indexed in the employed database, 11,521 were basic science papers (specifically, research with rodents, based on the used descriptors), which amounts to 12.9% of the total. In 2009, 798 works were completed in basic sleep research, representing a 78% increase compared to 2000 and a 706% increase compared to 1990.

Although the worldwide growth in basic sleep research has been inferior to the overall growth in research on the subject, prominence of in the worldwide sleep research scene is greater within the basic science realm. The Brazilian body of basic science sleep research is responsible for 3.61% (416 publications) of the worldwide production, ranking 8th in terms of publication numbers. If considering only 2009, Brazil takes the 5th place, as it is responsible for 6.14% of the worldwide production.

SLEEP AND BASIC SCIENCE BEHAVIORAL RESEARCH

Descriptors: “Sleep” AND (“animals” OR “rat” OR “rats” OR “mice” OR “mouse”) AND “behavior”
The sleep-related body of basic science research, when restricted to studies that focus on behavior, contains 1,557 indexed publications, with an accentuated productivity increase beginning in the 1990s. This increase continues today, with a worldwide production of 115 publications in 2009, a 51.3% increase over the year 2000.

In the 1990s, when worldwide animal behavior research on sleep exhibited the above-mentioned increase, the Brazilian research program was just beginning and was still internationally insignificant. However, the Brazilian research in this field is currently highly relevant, and Brazil is the 3rd most productive country, responsible for 7.25% of the total worldwide production and for 6.95% of the 2009 worldwide production. This great Brazilian presence in the international arena tends to persist when individual behaviors are analyzed, as will be noted below.

SLEEP AND BASIC RESEARCH ON STRESS

Descriptors: “Sleep” AND (“animals” OR “rat” OR “rats” OR “mice” OR “mouse”) AND “stress”
The worldwide production of basic sleep research related to stress is consistent with the trends described above. A considerable increase in the publication number is noted from 1990 to the present. In total, 1,123 works on the subject are indexed, with 146 published in 2009.

Brazil has the 4th greatest publication number in this field, tallying 87 papers, which corresponds to 7.75% of the total. The Brazilian publication trend follows that of the worldwide increase, but on a smaller scale, with 12 publications each in 2008 and 2009, when it ranked 2nd in terms of publication numbers.

SLEEP AND BASIC RESEARCH ON DEPRESSION

Descriptors: “Sleep” AND (“animals” OR “rat” OR “rats” OR “mice” OR “mouse”) AND “depression”
The worldwide body of researchers has been extremely productive in the study of sleep and depression since the be-
ginning of the 1990s, with 50 indexed publications in 2009 and an observed peak of 71 publications in 2007. Although the worldwide publication is extensive, the Brazilian participation is not as prominent as it is with other analyzed behaviors. Brazil occupies the 10th position for publication numbers in this field, being responsible for 3.15% of the total.

SLEEP AND BASIC RESEARCH ON ANXIETY
Descriptors: “Sleep” AND (“animals” OR “rat” OR “mice” OR “mouse”) AND “anxiety”

The worldwide research body on sleep and anxiety in animals laboratory was largely established in the mid-1990s, after which a rapid increase in publication numbers occurred. While in 2000 there were only 11 studies on the subject, in 2008 there were 40 and in 2009 there were 30 articles published.

Brazil, as with basic science behavior and sleep studies in general, plays a significant role in the basic research that is related to sleep and anxiety behavior. The Brazilian production is equivalent to 7.8% of the worldwide production, ranking 3rd in the number of publications on the subject.

SLEEP AND BASIC RESEARCH ON SEXUAL BEHAVIOR
Descriptors: “Sleep” AND (“animals” OR “rat” OR “mice” OR “mouse”) AND “sexual” AND “behavior”

Worldwide, basic research on sleep and sexual behavior has shown little growth over two decades. Although it began to gain momentum as a research field in the 1990s, it never passed the mark of 15 annual publications, having indexed a total of only 130 works. However, although the volume of publications concerning this specific behavior is not large, the representation of Brazil is notable, as it is the 2nd biggest contributor in terms of publications on the subject. The Brazilian production accounts for 30.77% of the overall publications on sexual behavior and sleep. The year 2007 is particularly notable, as Brazil was the country with the greatest contribution in this year, with 69.23% of publications, a feat that was repeated in 2009.

SLEEP AND BASIC RESEARCH ON FEEDING BEHAVIOR
Descriptors: “Sleep” AND (“animals” OR “rat” OR “mice” OR “mouse”) AND “feeding behavior”

There are 112 publications on sleep and feeding behavior that are indexed in the consulted database. These publications follow an erratic temporal pattern, with unstable worldwide production, varying between 6 and 16 works per year in the last decade, with successive increases and decreases in publication numbers during these years. Amongst these papers, 16 are Brazilian, which accounts for 14.29% of the total. Although Brazilian participation is expansive in this field, there is no observed increase in publication numbers over time, with a maximum number of publications of three per year in both 2006 and 2008. Nevertheless, Brazilian research on sleep and feeding behavior ranks 3rd worldwide.

SLEEP AND BASIC RESEARCH ON AGGRESSIVE BEHAVIOR
Descriptors: “Sleep” AND (“animals” OR “rat” OR “mice” OR “mouse”) AND (“behavior aggression” OR “aggressive”)

Worldwide, the basic science research on the relationship between aggressive behavior and sleep is limited, but it has been consistent since research began on this topic in the middle of the 1980s. In total, only 69 studies are indexed. Among this small publication number, the Brazilian participation is notable, with 9 publications, accounting for 13.04% of the total. In this field, Brazil is the 2nd most productive country in terms of publication numbers.

SLEEP AND BASIC RESEARCH ON MATERNAL BEHAVIOR
Descriptors: “Sleep” AND (“animals” OR “rat” OR “mice” OR “mouse”) AND “maternal” AND “behavior”

Among all analyzed behaviors, basic science research on the relationship between sleep and maternal behavior was the most limited. Only nine works are indexed in the database, and none have come from Brazilian researchers.

The global and Brazilian evolution of sleep publications in general and in basic science research is presented in Figure 1. Figure 2 presents the global and Brazilian evolution of research on sleep broken down by the described behaviors. Table 1 presents descriptive statistics pertaining

Figure 1: General and basic science production about sleep from 1940 to 2010, both in worldwide and Brazil. The vertical axis was broken into two disproportionate segments to better data visualization. General production refers to the total publication production pertaining to sleep in the considered period, encompassing both clinical and basic research. Basic research refers to animal research on sleep, with the research being completed with rodents as animal models.
Behavioral research and sleep in Brazil
to publications on sleep and the described behaviors, and Table 2 presents the ranking of the most productive countries in terms of basic science research on sleep and the listed behaviors.

DISCUSSION
The present study aimed to propose an overview and to demonstrate, in a synthetic manner, the current evolution of the Brazilian and worldwide basic behavioral sleep research. However, for an appropriate discussion of the presented data, some considerations must be raised. It is noted that the results do not necessarily reflect all of the publications on the examined subjects, but rather the total indexed publications in the analyzed database (Web of Knowledge). Although the information was obtained from a database with international prestige and broad coverage, it is not possible to guarantee that all publications on the subject are accessible in this manner. Moreover, it is emphasized that the presented data pertain only to studies that were found in searches that used the terms noted above. Changes in the search terms can result in substantial changes in the publications that are found. However, even with the cited caveats, the search results seem to satisfactorily reflect the actual situation surrounding the researched topics. Finally, one must remember the focus of this article: basic science research in the field of sleep and behavior using animal models, specifically rodents.

A clear increase, beginning in the early 1990s, is noted herein with regard to the worldwide scientific production of both basic science and overall research on sleep. A similar increase is also noted when just Brazilian research is examined; however, the Brazilian increase is delayed slightly, between the end of the 1990s and the beginning of the 2000s. An increase in the Brazilian participation relative to the

Table 1: Brazilian and world production between the years 2000 and 2009, regarding the addressed behaviors. The Brazilian participation in relation to world production is presented in percentages

<table>
<thead>
<tr>
<th></th>
<th>World</th>
<th>Brazil</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total production</td>
<td>Production in 2009</td>
</tr>
<tr>
<td>Sleep (general analysis)</td>
<td>89,202</td>
<td>3,242</td>
</tr>
<tr>
<td>Sleep and basic research</td>
<td>11,52</td>
<td>446</td>
</tr>
<tr>
<td>Sleep and behavior research</td>
<td>1,157</td>
<td>76</td>
</tr>
<tr>
<td>Sleep and stress</td>
<td>1,123</td>
<td>36</td>
</tr>
<tr>
<td>Sleep and depression</td>
<td>824</td>
<td>52</td>
</tr>
<tr>
<td>Sleep and anxiety</td>
<td>359</td>
<td>11</td>
</tr>
<tr>
<td>Sleep and sexual behavior</td>
<td>130</td>
<td>6</td>
</tr>
<tr>
<td>Sleep and feeding behavior</td>
<td>112</td>
<td>5</td>
</tr>
<tr>
<td>Sleep and aggressive behavior</td>
<td>69</td>
<td>2</td>
</tr>
<tr>
<td>Sleep and maternal behavior</td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 2: Temporal evolution of worldwide and Brazilian productivity in basic science research on sleep. The data refer to general behavioral research and research specifically on stress, depression, anxiety, sexual behavior and feeding behavior. Data on aggressive and maternal behavior are not presented due to low publication numbers. In all representations, the size of both axes was adjusted to the publication volume. It is notable that in all of the cases, there is a global trend of increased productivity; however, this finding becomes less evident when only Brazilian research is considered, as the production growth amplitude is decreased.
When analyzing Brazilian production in the behaviors examined separately, different results are obtained from those acquired in basic and overall research on sleep, in which Brazilian research followed the worldwide trends, although in a smaller degree and with a slight delay. In general, for the majority of the studied behaviors, the number of indexed publications did not exceed ten per year and did not demonstrate a clear increase with time, instead maintaining an erratic and irregular pattern in the annual publication number. This may be due to the recent increased Brazilian production on sleep in relation to worldwide production. Nonetheless, two of the analyzed behaviors differed from this pattern. The publications on stress and sleep seem to follow a trend of increased publication numbers, having maintained a stable average of more than 10 annual publications since 2006, and publications about sleep and sexual behavior stand out not for the volume of publications, but for the Brazilian representation within the worldwide production.

Table 2: Ranking of the countries with the greatest total scientific productivity in 2009, regarding sleep broken down by the assessed behaviors. The hyphens indicate that there was no corresponding production in the category in question. For example, in 2009 there were no publications about sleep and maternal behavior, and all publications on sleep and sexual behavior in 2009 were produced by only the four countries listed.

<table>
<thead>
<tr>
<th>Scientific production</th>
<th>1)</th>
<th>2)</th>
<th>3)</th>
<th>4)</th>
<th>5)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep (general analysis)</strong></td>
<td>U.S.A.</td>
<td>Canada</td>
<td>England</td>
<td>Germany</td>
<td>Brazil</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>Sleep and basic research</td>
<td>U.S.A.</td>
<td>England</td>
<td>Canada</td>
<td>Germany</td>
<td>Brazil</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Sleep and behavioral research</td>
<td>U.S.A.</td>
<td>Japan</td>
<td>Canada</td>
<td>France</td>
<td>Brazil</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Sleep and stress</td>
<td>U.S.A.</td>
<td>France</td>
<td>Japan</td>
<td>Brazil</td>
<td>Germany</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Sleep and depression</td>
<td>U.S.A.</td>
<td>Germany</td>
<td>Canada</td>
<td>France</td>
<td>Brazil</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Sleep and anxiety</td>
<td>U.S.A.</td>
<td>Germany</td>
<td>Canada</td>
<td>France</td>
<td>England</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Sleep and sexual behavior</td>
<td>U.S.A.</td>
<td>Brazil</td>
<td>Mexico</td>
<td>India</td>
<td>Canada</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Sleep and feeding behavior</td>
<td>Brazil</td>
<td>U.S.A.</td>
<td>Mexico</td>
<td>Japan</td>
<td>-</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Sleep and aggressive behavior</td>
<td>U.S.A.</td>
<td>Brazil</td>
<td>Japan</td>
<td>Holland</td>
<td>England</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Sleep and maternal behavior</td>
<td>U.S.A.</td>
<td>France</td>
<td>Italy</td>
<td>Belgium</td>
<td>Canada</td>
</tr>
<tr>
<td>Total 2009</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
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</table>

Overall production can also be seen over time, with the Brazilian contribution achieving great relevance in recent years. When considering basic behavioral sleep research, this same trend is maintained, with increased worldwide production beginning in the 1990s, and increased Brazilian contribution commencing in the following decade.

It is possible to clearly identify a similar increase in the number of worldwide publications in some of the analyzed behaviors, but not in all. Specifically, sleep relationship with stress, depression and anxiety behaviors presents evident growth in publication numbers with time, whereas its relationship with feeding and sexual behaviors showed less evident growth in the published article numbers. Finally, articles on sleep and aggressive and maternal behaviors did not show any increase in publication number over the years and never exceeded ten annual publications. These data evidence a possible lack of interest by the international scientific community in the relationship between sleep and these two underestimated behaviors.
Nevertheless, even though the volume of Brazilian publications referring to the analyzed behaviors seems not to have increased in recent years, the proportion of the Brazilian contribution is extremely important in the global context. For all of the analyzed behaviors, Brazil was ranked between 2nd and 10th; it is among the most productive nations and is becoming, in some specific cases (for example, the publications on “sleep and sexual behavior” in the years from 2007 to 2009), the most productive. In this context, Brazil often ranks ahead of countries that are well-known for scientific production, such as Germany, France, England and Japan, as noted in Table 2.

The data on Brazilian research, specifically for general, basic science and basic behavioral sleep research, are in accord with the observed increase in the Brazilian contribution to the fields of Psychiatry, Psychobiology and mental health\(^\text{12}\). Moreover, the importance of Brazilian basic research, especially research with experimental animals, has become increasingly evident\(^\text{13}\).

This increased importance of Brazilian sleep research on the global scale demonstrates the competence of the country in the dynamics of the acquisition and presentation of scientific data on the subject. One can see that there has been a large increase in the global understanding of various sleep-related factors over the last few decades, including genetics, neurophysiology, psychobiology and cellular biology\(^\text{14}\). As evidence of this worldwide trend beyond the data presented in this article, the increased number of global sleep-specialized journals about sleep can be cited. While in the beginning of the 1990s there was only 1 journal specifically dedicated to sleep research (Sleep), in 2004 there were already at least 16 specific journals on the subject\(^\text{15}\). Since then, the number of periodicals has grown even more, with other sleep journals having appeared, such as The Journal of Clinical Sleep Medicine, Sleep Medicine Clinics and Sleep Science.

Obviously, the emphasis of this article on Brazilian basic sleep research does not aim to detract from the importance of clinical sleep research and the other Brazilian research fields. Considering animal research as an important tool for the study of human sleep\(^\text{16}\) and considering the definition and importance of translational science\(^\text{17}\), both branches of sleep science – basic and clinical – interact and cooperate toward achieving the same goals.

In short, the present article aimed to propose a broad view on the importance and relevance of the Brazilian contribution to the published literature on sleep, specifically to the scientific production of basic sleep behavior research. The presented data demonstrate the importance of Brazilian basic science research in the field of sleep research, the participation of the country in the worldwide production on this subject and the adequacy of the outputs of this research field, which are increasing both in volume and publication relevance.

REFERENCES