

# Possible Cognitive Benefits of Acute Physical Exercise in Children With ADHD: A Systematic Review

Journal of Attention Disorders  
2017, Vol. 21(5) 367–371  
© The Author(s) 2014  
Reprints and permissions:  
sagepub.com/journalsPermissions.nav  
DOI: 10.1177/1087054714526041  
journals.sagepub.com/home/jad



Viviane Grassmann<sup>1</sup>, Marcus Vinicius Alves<sup>1</sup>, Ruth Ferreira Santos-Galduróz<sup>2,3</sup>, and José Carlos Fernandes Galduróz<sup>1</sup>

## Abstract

**Objective:** Studies have suggested that even a single session of physical exercise enhances executive functions. ADHD is among the most common developmental disorders in childhood, but little is known about alternative treatments for this disorder. Therefore, we performed a systematic review of the literature to analyze articles that evaluated the executive functions of children with ADHD after an acute exercise session. **Method:** We reviewed articles indexed in the PubMed, American Psychiatric Association (APA) psychNET, Scopus, and Web of Knowledge databases between 1980 and 2013. **Results:** Of 231 articles selected, only three met the inclusion criteria. **Conclusion:** Based on these 3 articles, we concluded that 30 min of physical exercise reportedly improved the executive functions of children with ADHD. Due to the small number of articles selected, further studies are needed to confirm these benefits. (*J. of Att. Dis.* 2017; 21(5) 367-371)

## Keywords

acute exercise, ADHD, children, cognitive functions, physical exercise

## Introduction

Physical exercise is important at any age, as it is beneficial to health and quality of life, enhances self-esteem, and improves cognitive functions (CF; American College of Sports Medicine, 2006; Chang & Etner, 2009).

Physically active children are reported to have better academic performance (Castelli, Hillman, Buck, & Erwin, 2007). Katz et al. (2010) observed that children with ADHD who performed physical exercises in class had reductions in the medications taken for ADHD.

Apparently, physical exercise provides beneficial effects on the CF of children who have learning disorders, such as ADHD. Some studies have shown that regular physical exercise can improve many areas of behavior in children with ADHD (Smith et al., 2013; Verret, Guay, Berthiaume, Gardiner, & Béliveau, 2012).

ADHD is the most common disorder in the world, with a prevalence of 6.5% to 11% in children between 5 and 15 years of age (Faraone, Sergeant, Gillberg, & Biederman, 2003). ADHD occurs due to neurobiological alterations, mainly regarding the dysfunction of dopaminergic transmission in structures such as the striatum and the frontal lobe (Vaidya et al., 1998). These alterations impair executive functions, such as motor control, working memory, and

inhibitory control (Schneider, Retz, Coogan, Thome, & Rösler, 2006). The main signs and symptoms of this disorder are impulsivity, hyperactivity, and inattention (American Psychiatric Association [APA], 1994; World Health Organization [WHO], 1993).

Methylphenidate (MTP) and amphetamines are the medications usually prescribed as a treatment for this type of disorder (Hodgkins, Shaw, Coghil, & Hechtman, 2012). It is widely recognized that physical exercise also enhances nor-adrenaline and dopamine concentrations in the encephalon. Meeusen et al. (1997) detected increases in these neurotransmitters in the striatum of rats after 60 min of physical exercise. Moreover, this activity also increased the serum levels of calcium, activating the calmodulin-dependent system and consequently enhancing dopamine synthesis (Sutoo & Akiyama, 2003). Therefore, physical exercise might represent an

<sup>1</sup>Universidade Federal de São Paulo, Brazil

<sup>2</sup>Universidade Federal do ABC, Santo André, Brazil

<sup>3</sup>Universidade Estadual Paulista, São Paulo, Brazil

## Corresponding Author:

José Carlos Fernandes Galduróz, Department of Psychobiology, Universidade Federal de São Paulo, Rua Napoleão de Barros, 925, CEP 04024-002, São Paulo, Brazil.

Email: galduroz@unifesp.br

alternative treatment for these children (Medina et al., 2010). Thus, the aim of this systematic review was to study the effects of acute physical exercise in children with ADHD.

## Method

The databases used to search articles published between 1980 and 2013 were PubMed, APA PsycNET, Scopus, and Web of Science. We selected controlled studies in English that evaluated the cognitive effects of an acute exercise session in children with ADHD. The inclusion criteria were original and controlled studies that evaluated the effects of one session of physical exercise on the CF of children with ADHD. Therefore, we used the following Boolean descriptors: (adhd OR "attention deficit disorder" OR "attention deficit hyperactivity disorder" OR "attention-deficit/hyperactivity disorder") AND (exercise OR "physical exercise" OR "aerobic exercise" OR "resistance exercise" OR "anaerobic exercise" OR "acute exercise" OR sport) AND humans.

We selected three studies of the 310 found (Table 1). We excluded 129 papers that were not original, 20 papers that did not evaluate children with ADHD, 45 papers that did not involve physical exercise, 66 papers that evaluated neither children with ADHD nor physical exercise, 3 studies that evaluated animals, 4 studies that were conducted in adults, 18 studies that did not assess the effects of physical exercise on CF, 11 papers that evaluated the effects of physical training but did not evaluate the effects of acute physical exercise, and 11 papers that were written in a language other than English, Spanish, or Portuguese.

## Results

The first study involved 31 hyperactive children (18 or greater on the Conners Abbreviated Teacher Rating Scale [CATRS]) and 31 children without hyperactivity (less than 4 on the Conners scale). All of the participants exercised on an ergometric bicycle at a heart rate of 170 beats per minute (BPM). The results showed no differences as a function of the duration of the exercise in any of the groups (Craft, 1983).

The other two studies, however, showed improvement in cognition after exercise. Medina et al. (2010) evaluated the effects of acute physical exercise in children with ADHD who were taking medications for that condition and children who were not. All of the children performed interval training on a treadmill for 30 min. The protocol had 10 loads of 2 min of high to moderate activity and 1 min of rest. The children were asked not to take their medicines for 48 hr before the evaluation. The results were interpreted as representing that children with ADHD (users or non-users of MTP) had improved vigilance and reaction time and decreased impulsivity, and had better stability in all measurements after physical exercise, compared with their basal evaluations. There were no significant differences between users and non-users of MTP (Medina et al., 2010).

Chang, Liu, Yu, and Lee (2012) recruited 40 children diagnosed with ADHD by a psychiatrist. They were randomly assigned to two groups: exercise and control. The first group ran on a treadmill for 30 min (5 min warm-up, 20 min main exercise, and 5 min cool down) at 50% to 70% of the heart rate reserve, indicating moderate intensity. The second group watched a running/exercise-related video for the same duration. The authors showed greater facility on the Stroop Color-Word test (inhibitory control and selective attention), fewer non-perseverative errors (problem solving) and improvement in categories they completed (set shifting) on the Wisconsin Card Sorting Test (WCST) after exercise. Fifty percent of the participants were taking medications for ADHD, but the authors did not describe whether they had taken them on the evaluation day.

## Discussion

The present review suggests possible positive effects of acute exercise on the CF of children with ADHD, particularly on impulsivity, vigilance, reaction time, inhibitory control, selective attention, and problem solving, as well as a slight improvement in set shifting.

The three studies evaluated physical training of moderate to high intensity, which, according to the literature, appears to be the ideal intensity for improvement in CF to occur (Córdova, Silva, Moraes, Simões, & Nóbrega, 2009; Hillman et al., 2009). However, the training duration proposed by Craft (1983) might have been overly short (1, 5, or 10 min), thus possibly not sufficient to yield a significant effect on the improvement in CF. The training period analyzed by Chang et al. (2012) and Medina et al. (2010), that is, 30 min, was similar to the 20-min training that previous studies have postulated as having a beneficial effect on CF (Córdova et al., 2009; Hillman et al., 2009). Hillman et al. (2009) evaluated children without ADHD and free of neurological diseases, observing that 20 min of aerobic exercise at a moderate to high intensity could improve attentional control and academic performance. A study performed in elderly women evaluated the effect of 25 min of physical exercise at three intensities (60%, 90%, and 110% of the anaerobic threshold). It revealed a significant improvement in executive functions and alertness after physical exercise performed at 90% of the threshold. After exercise at the intensity of 110%, there was improvement only regarding verbal fluency, whereas at 60%, there were no differences (Córdova et al., 2009). Such results suggest that moderate to high intensities might provide benefits for CF. At exhausting intensities, in contrast, this benefit might decrease or even disappear.

Physical exercise seems to improve CF through increases in some neurotransmitters, as well as by means of the liberation of some growth factors, such as insulin growth factor-1 (IGF-1) and brain-derived neurotrophic factor (BDNF; Cassilhas et al., 2007; Coelho et al., 2013; Ding, Vaynman, Akhavan, Ying, & Gomez-Pinilla, 2006; Meeusen et al., 1997).

**Table 1.** Review of the Articles Selected.

	Authors		
	Craft (1983)	Medina et al. (2010)	Chang, Liu, Yu, and Lee (2012)
N; % of male; age	31 with ADHD and 31 without ADHD; 100; 7-10	25; 100; 7-15	40; 92.5; 8-13
Diagnosis; Medication	School psychologist (18 or more on the CATRS); did not take medication	Multidisciplinary; MTP (15 volunteers 5 to 10 mg/day; one volunteer 30 mg); and carbamazepine, valproic acid and lamotrigine/MTP was withdrawn 48 hr prior to the test day	Psychiatric physician; 50% of each group were under medication for ADHD/not reported whether medication was withdrawn prior to the test day
Subtype; Comorbidities	Not described; no reports of severe emotional disorders or brain damage	Not described; psychiatric comorbidities, asthma, and rhinitis	14 inattentive, 21 combined, 5 impulsive/hyperactive, and 20 under medication (10 in each group); not described.
Level of physical activity; $\dot{V}O_2$ Max	Not described; not described	Not described (the most common recreational activities were as soccer and cycling); US ( $43.80 \pm 7.75$ ml/kg/min) and NUS ( $43.36 \pm 5.21$ ml/kg/min)	Not described; maximum estimated by formula
Groups; Controls	With ADHD and without ADHD; did not apply	US and NUS; stretching	With and without exercise; watched a video about running and exercises
Type of exercise; Intensity; Duration	Ergometric bicycle; moderate to high (170 bpm); 0, 1, 5, 10 min	Treadmill (intervals); moderate to high; 30 min: 10 min $\times$ 2 min and 1 min of rest	Treadmill (aerobic); moderate to high (50%-70% HRR); 30 min (5 min warm up; 20 min exercise; 5 min cool down)
Cognitive evaluation	Digit Span (WISC-R); Coding B (WISC-R); ITPA; Visual Sequential Memory	CPT	STROOP test; Wisconsin Card Sorting Test
Results	The duration of physical exercise did not have any effects on the cognitive performances of either hyperactive or non-hyperactive children; no inverted U curve	Both groups (with and without medication) showed improvement in vigilance, reaction time, stability, and impulsivity after exercise, when compared with their own basal levels; no significant differences between groups (US and NUS) after exercise	Better performance in the Stroop color-word after exercise/ improvement in the perseverative errors and in the categories completed of the WCST after exercise; no effect of exercise on the Stroop word and Stroop color tests or on total correct, perseverative response, perseverative errors, conceptual level response

Note. CATRS = Conners Abbreviated Teacher Rating Scale; CPT = Continuous Performance Test; HRR = heart rate reserve; MTP = methylphenidate; US = users of methylphenidate; NUS = non-users of methylphenidate; WISC-R = Wechsler Intelligence Scale for Children-Revised; ITPA = Illinois Test of Psycholinguistic Abilities.

Medina et al. (2010) observed cognitive improvements in children who used MTP and in those who did not; thus, the authors concluded that the improvement could not be associated with the increase in catecholamine, because it was detected both groups. This explanation is questionable, however, because the children who used MTP had the medication suspended 48 hr prior to the tests. Medications that aim to improve ADHD symptoms, as is the case with MTP, increase the extracellular concentrations of dopamine and noradrenaline in the brain (Kuczenski & Segal, 1997), and they last for 4 hr for the short-half-life formulations and

from 7 to up to 12 hr for the long half-life agents, while the amphetamines that have similar effects also last from 4 to 14 hr, depending on the formulation (Hodgkins et al., 2012).

Chang et al. (2012) did not report whether the medications, which half of the sample were taking, were withdrawn before their study was performed. This information is crucial, considering that medication may mask the effects of exercise. Robinson, Eggleston, and Bucci (2012) compared the effects of MTP, atomoxetine, and/or physical exercise on the behavior of spontaneously hypertensive rats, and they reported that all three forms of treatment were effective in reducing inattention.

Nevertheless, the combination of exercise and medication was not more effective than each treatment modality alone, which suggests that the three act through similar mechanisms.

Physical exercise can also increase the release of growth factors, enhancing the levels of IGF-1 and of BDNF, thereby improving CF (Cassilhas et al., 2007; Ding et al., 2006). To the best of our knowledge, there have been no studies that have evaluated the effects of acute physical exercise on the BDNF of children. In adults and elderly individuals, however, acute physical exercise at moderate intensity can increase the serum levels of BDNF (Coelho et al., 2013; Ferris, Williams, & Shen, 2007; Laske et al., 2010). Although this fact does not seem to be related to improvement in cognition in the short term, the repeated increase in BDNF during regular exercise practice might bring some benefit over the long term (Ferris et al., 2007).

Both Medina et al. (2010) and Chang et al. (2012) used positive controls, children who would report to the laboratory and perform some activity (stretching or watching a video). This fact is important to eliminate the possibility that the effect was due to a change in routine, thus preventing the Hawthorne effect that refers to the changes in people's behavior after close monitoring (Davis & Feldman, 2013).

According to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; APA, 2013), ADHD is divided into three subtypes: inattentive, hyperactive/impulsive, and combined (APA, 1994). Only Chang et al. (2012) reported the subtypes in their sample and declared that there were no significant differences among the subtypes. Another aspect regards comorbidities. The sample of Craft (1983) involved no other comorbidities, such as severe emotional disorders or brain damage. It is essential that future studies disclose the comorbidities and subtypes because there might be a greater effect on attention in groups that involve larger numbers of inattentive individuals or on impulsivity in groups in which there are larger numbers of hyperactive children, as well as enhancement in other aspects (e.g., mood) related to the comorbidities that influence CF.

Future studies should report levels of previous physical activity because long-term aerobic training might enhance the effects of acute physical exercise on CF (Pesce, Cereatti, Forte, Crova, & Casella, 2011). Moreover, they should also evaluate the duration of the effects after exercise, as Pontifex, Hillman, Fernhall, Thompson, and Valentini (2009) suggested possible improvements in working memory and reaction time after aerobic exercise that remained for at least 30 min. Another study also showed an improvement in CF (planning) after 30 min of aerobic exercise in adults, which lasted at least 80 min after the cessation of exercise (Hung, Tsai, Chen, Wang, & Chang, 2013). Therefore, post-exercise evaluations at different time points might indicate effective changes in the CF of children.

In conclusion, 30 min of moderate- to high-intensity physical exercise may improve the CF of children with ADHD. However, due to the small number of studies in this

area, we cannot reach a satisfactory conclusion, which indicates the need for further investigations to be undertaken.

### Acknowledgments

The authors express gratitude to the institutions that made this article possible: AFIP (Associação Fundo de Incentivo a Pesquisa), FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo), CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico), and FADA (Fundo de Auxílio aos docentes e Alunos)—Universidade Federal de São Paulo.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This article received funding for research from FAPESP (2011/08387-6), AFIP, and CNPq.

### References

- American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington, DC: Author.
- American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). Washington, DC: Author.
- American College of Sports Medicine. (2006). Guidelines for exercise testing and prescription. M. H. Whaley, P. H. Brubaker, and R. M. Otto (Eds.). Philadelphia, PA: Lea and Febiger.
- Cassilhas, R. C., Viana, V. A., Grassmann, V., Santos, R. T., Santos, R. F., Tufik, S., & Mello, M. T. (2007). The impact of resistance exercise on the cognitive function of the elderly. *Medicine & Science in Sports & Exercise*, *39*, 1401-1407.
- Castelli, D. M., Hillman, C. H., Buck, S. M., & Erwin, H. E. (2007). Physical fitness and academic achievement in third- and fifth-grade students. *Journal of Sport & Exercise Psychology*, *29*, 239-252.
- Chang, Y. K., & Etnier, J. L. (2009). Effects of an acute bout of localized resistance exercise on cognitive performance in middle-aged adults: A randomized controlled trial study. *Psychology of Sport and Exercise*, *10*, 19-24.
- Chang, Y. K., Liu, S., Yu, H. H., & Lee, Y. H. (2012). Effect of acute exercise on executive function in children with attention deficit hyperactivity disorder. *Archives of Clinical Neuropsychology*, *27*, 225-237. doi:10.1093/arclin/acr094
- Coelho, F. G., Gobbi, S., Andreatto, C. A., Corazza, D. I., Pedrosa, R. V., & Santos-Galduróz, R. F. (2013). Physical exercise modulates peripheral levels of brain-derived neurotrophic factor (BDNF): A systematic review of experimental studies in the elderly. *Archives of Gerontology and Geriatrics*, *56*, 10-15. doi:10.1016/j.archger.2012.06.003
- Córdova, C., Silva, V. C., Moraes, C. F., Simões, H. G., & Nóbrega, O. T. (2009). Acute exercise performed close to the anaerobic threshold improves cognitive performance in elderly females. *Brazilian Journal of Medical and Biological Research*, *42*, 458-464.

- Craft, D. H. (1983). Effect of prior exercise on cognitive performance tasks by hyperactive and normal young boys. *Perceptual & Motor Skills, 56*, 979-982.
- Davis, S. A., & Feldman, S. R. (2013). Using Hawthorne effects to improve adherence in clinical practice: Lessons from clinical trials. *JAMA Dermatology, 149*, 490-491. doi:10.1001/jama-dermatol.2013.2843
- Ding, Q., Vaynman, S., Akhavan, M., Ying, Z., & Gomez-Pinilla, F. (2006). Insulin-like growth factor I interfaces with brain-derived neurotrophic factor-mediated synaptic plasticity to modulate aspects of exercise-induced cognitive function. *Neuroscience, 140*, 823-833.
- Faraone, S. V., Sergeant, J., Gillberg, C., & Biederman, J. (2003). The worldwide prevalence of ADHD: Is it an American condition? *World Psychiatry, 2*, 104-113.
- Ferris, L. T., Williams, J. S., & Shen, C. L. (2007). The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. *Medicine & Science in Sports & Exercise, 39*, 728-734.
- Hillman, C. H., Pontifex, M. B., Raine, L. B., Castelli, D. M., Hall, E. E., & Kramer, A. F. (2009). The effect of acute treadmill walking on cognitive control and academic achievement in preadolescent children. *Neuroscience, 159*, 1044-1054. doi:10.1016/j.neuroscience.2009.01.057
- Hodgkins, P., Shaw, M., Coghill, D., & Hechtman, L. (2012). Amphetamine and methylphenidate medications for attention-deficit/hyperactivity disorder: Complementary treatment options. *European Child & Adolescent Psychiatry, 21*, 477-492. doi:10.1007/s00787-012-0286-5.
- Hung, T. M., Tsai, C. L., Chen, F. T., Wang, C. C., & Chang, Y. K. (2013). The immediate and sustained effects of acute exercise on planning aspect of executive function. *Psychology of Sport and Exercise, 14*, 728-736.
- Katz, D. L., Cushman, D., Reynolds, J., Njike, V., Treu, J. A., Walker, J., . . . Katz, C. (2010). Putting physical activity where it fits in the school day: Preliminary results of the ABC (Activity Bursts in the Classroom) for fitness program. *Preventing Chronic Disease, 7*(4), A82.
- Kuczenski, R., & Segal, D. S. (1997). Effect of methylphenidate on extracellular dopamine, serotonin and norepinephrine: Comparison with amphetamine. *Journal of Neurochemistry, 68*, 2032-2037.
- Laske, C., Bansbach, S., Stransky, E., Bosch, S., Straten, G., Machann, J., . . . Eschweiler, G. W. (2010). Exercise-induced normalization of decreased BDNF serum concentration in elderly women with remitted major depression. *International Journal of Neuropsychopharmacology, 13*, 595-602. doi:10.1017/S1461145709991234
- Medina, J. A., Netto, T. L., Muszkat, M., Medina, A. C., Botter, D., Orbetelli, R., . . . Miranda, M. C. (2010). Exercise impact on sustained attention of ADHD children, methylphenidate effects. *Attention Deficit Hyperactivity Disorder, 2*, 49-58. doi:10.1007/s12402-009-0018-y
- Meusen, R., Smolders, I., Sarre, S., de Meirleir, K., Keizer, H., Serneels, M., . . . Michotte, Y. (1997). Endurance training effects on neurotransmitter release in rat striatum: An in vivo microdialysis study. *Acta Physiologica Scandinavica, 159*, 335-341.
- Pesce, C., Cereatti, L., Forte, R., Crova, C., & Casella, R. (2011). Acute and chronic exercise effects on attentional control in older road cyclists. *Gerontology, 57*, 121-128. doi:10.1159/000314685
- Pontifex, M. B., Hillman, C. H., Fernhall, B., Thompson, K. M., & Valentini, T. A. (2009). The effect of acute aerobic and resistance exercise on working memory. *Medicine & Science in Sports & Exercise, 41*, 927-934. doi:10.1249/MSS.0b013e3181907d69
- Robinson, A. M., Eggleston, R. L., & Bucci, D. J. (2012). Physical exercise and catecholamine reuptake inhibitors affect orienting behavior and social interaction in a rat model of attention-deficit/hyperactivity disorder. *Behavioral Neuroscience, 126*, 762-771. doi:10.1037/a0030488
- Schneider, M., Retz, W., Coogan, A., Thome, J., & Rösler, M. (2006). Anatomical and functional brain imaging in adult attention-deficit/hyperactivity disorder (ADHD)—A neurological view. *European Archives of Psychiatry and Clinical Neuroscience, 256*(1), i32-i41.
- Smith, A. L., Hoza, B., Linnea, K., McQuade, J. D., Tomb, M., Vaughn, A. J., . . . Hook, H. (2013). Pilot physical activity intervention reduces severity of ADHD symptoms in young children. *Journal of Attention Disorders, 17*, 70-82. doi:10.1177/1087054711417395
- Sutoo, D., & Akiyama, K. (2003). Regulation of brain function by exercise. *Neurobiology of Disease, 13*, 1-14.
- Vaidya, C. J., Austin, G., Kirkorian, G., Ridlehuber, H. W., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. E. (1998). Selective effects of methylphenidate in attention deficit hyperactivity disorder: A functional magnetic resonance study. *Proceedings of the National Academy of Sciences, 95*, 14494-14499.
- Verret, C., Guay, M. C., Berthiaume, C., Gardiner, P., & Béliveau, L. (2012). A physical activity program improves behavior and cognitive functions in children with ADHD: An exploratory study. *Journal of Attention Disorders, 16*, 71-80. doi:10.1177/1087054710379735
- World Health Organization. (1993). Classification of mental and behavioral disorders in CID-10 clinical descriptions and diagnostic guidelines. Porto Alegre, Brazil: Artes Médicas Editor.

## Author Biographies

**Viviane Grassmann**, MsC, is a Physical Educator, with subspecialty in psychobiology of physical exercise. She is making her doctorate at Psychobiology Department- Universidade Federal de São Paulo, Brazil. Her research focus is on the effects of physical training and polyunsaturated fatty acids in ADHD children.

**Marcus Vinicius Alves**, MsC, is a Psychologist and a PhD candidate at Psychobiology Department- Universidade Federal de São Paulo, Brazil. His primary research focus is on cognitive effort, memory consolidation and forgetting, in addition to the broader aspects of cognitive psychology and neuropsychology.

**Ruth Ferreira Santos-Galduróz**, MsC, PhD, is a Psychologist and a professor at Center of Mathematics, Computing and Cognition, Universidade Federal do ABC, Brazil.

**José Carlos Fernandes Galduróz**, MD, MsC, PhD, is a Psychiatrist and a professor at Psychobiology Department- Universidade Federal de São Paulo, Brazil.