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# Etude du Neurofeedback électroencéphalographique appliqué au trouble du déficit de l'attention avec ou sans hyperactivité

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Devant un jury composé de :

Prénom Nom, titre [ex. : Maître de conférence], établissement, rôle par rapport à la thèse  
[ex : Rapporteur, Président ou encore directeur de thèse]



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*A mon cher grand-père, René Marty.*



# REMERCIEMENTS

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# RESUME DE THESE

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**Mots-clés**





# ABSTRACT

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## Keywords



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# Chapitre 1

## Introduction

### 1.1 Définition du Neurofeedback

#### 1.1.1 Historique

Découverte de l'EEG, premiers pas de la neuromodulation avec Durup et Fressard, les études de Serman et Lubar, la très forte augmentation des études sur le Neurofeedback depuis les années 2000

#### 1.1.2 Principe du Neurofeedback

Conditionnement opérant, définition phase de transfert, type de seuillage, individualisation des protocoles (iapf), montage, matériel utilisé, marquage CE ou non, gestion des artefacts, définition neuromarqueur, définition impédance

### 1.2 Les champs d'application du Neurofeedback

#### 1.2.1 De nombreuses applications

Epilepsie, diminution de l'anxiété, douleurs chroniques, etc

#### 1.2.2 Neurofeedback et Trouble du Déficit de l'Attention avec ou sans Hyperactivité (TDAH)

Définition TDAH chez l'enfant (parler du dsm-4 et 5) et parler de l'essor de la problématique du TDAH chez l'adulte, parler des études et des méta-analyses sham-NFB

Enoncé de la problématique quant à l'efficacité du NFB appliqué aux enfants TDAH

## **1.3 Contribution et résumé des chapitres**

Lister les objectifs de la thèse : - Réplication et mise à jour d'une méta analyse en codant les étapes en Python - Identification des facteurs ayant une influence sur le NFB grâce à des méthodes multivariées - Analyse de la distribution d'un marqueur de l'attention pour augmenter l'efficacité du NFB

## **1.4 Liste des publications**

## Chapitre 2

# Evaluation de l'efficacité du Neurofeedback par la méta-analyse

## Chapitre 3

### Identification des facteurs influençant l'efficacité du Neurofeedback

## Chapitre 4

Analyse de la distribution d'un  
marqueur de l'attention au sein  
d'une population d'enfants TDAH



# Bibliographie

- P.-M. Aggensteiner, D. Brandeis, S. Millenet, S. Hohmann, C. Ruckes, S. Beuth, B. Albrecht, G. Schmitt, S. Schermuly, S. Wörz, et al. Slow cortical potentials neurofeedback in children with adhd : comorbidity, self-regulation and clinical outcomes 6 months after treatment in a multicenter randomized controlled trial. *European child & adolescent psychiatry*, 28(8) :1087–1095, 2019.
- O. Alkoby, A. Abu-Rmileh, O. Shriki, and D. Todder. Can we predict who will respond to neurofeedback? a review of the inefficacy problem and existing predictors for successful eeg neurofeedback learning. *Neuroscience*, 2017. doi : 10.1016/j.neuroscience.2016.12.050.
- L. E. Arnold, N. Lofthouse, S. Hersch, X. Pan, E. Hurt, B. Bates, K. Kassouf, S. Moone, and C. Grantier. Eeg neurofeedback for attention-deficit/hyperactivity disorder : Double-blind sham-controlled randomized pilot feasibility trial. *Journal of Attention Disorder*, 2014. doi : 10.1177/1087054712446173.
- M. Arns, S. de Ridder, U. Strehl, M. Breteler, and A. Coenen. Efficacy of neurofeedback treatment in adhd : the effects on inattention, impulsivity and hyperactivity : a meta-analysis. *Clinical EEG and neuroscience*, 40(3) :180–189, 2009. doi : 10.1177/155005940904000311.
- M. Arns, H. Heinrich, and U. Strehl. Evaluation of neurofeedback in adhd : the long and winding road. *Biological psychology*, 95 :108–115, 2014. doi : 10.1016/j.biopsycho.2013.11.013.
- A. R. Bakhshayesh, S. Hänsch, A. Wyschkon, M. J. Rezai, and G. Esser. Neurofeedback in adhd : a single-blind randomized controlled trial. *European child & adolescent psychiatry*, 20(9) :481, 2011. doi : 10.1007/s00787-011-0208-y.
- S. Baumeister, I. Wolf, N. Holz, R. Boecker-Schlier, N. Adamo, M. Holtmann, M. Ruf, T. Banaschewski, S. Hohmann, and D. Brandeis. Neurofeedback training effects on inhibitory brain activation in adhd : A matter of learning? *Neuroscience*, 2016. doi : 10.1016/j.neuroscience.2016.09.025.
- O. M. Bazanova, T. Auer, and E. A. Sapina. On the efficiency of individualized

- theta/beta ratio neurofeedback combined with forehead emg training in adhd children. *Frontiers in human neuroscience*, 12 :3, 2018.
- M. Beauregard and J. Levesque. Functional magnetic resonance imaging investigation of the effects of neurofeedback training on the neural bases of selective attention and response inhibition in children with attention-deficit/hyperactivity disorder. *Applied psychophysiology and biofeedback*, 31 (1) :3–20, 2006. doi : 10.1007/s10484-006-9001-y.
- M. Bink, C. van Nieuwenhuizen, A. Popma, I. L. Bongers, and G. J. M. van Boxtel. Behavioral effects of neurofeedback in adolescents with adhd : a randomized controlled trial. *European Child and Adolescent Psychiatry*, 2014. doi : 10.1007/s00787-014-0655-3.
- S. Bioulac, D. Purper-Ouakil, T. Ros, H. Blasco-Fontecilla, M. Prats, L. Mayaud, and D. Brandeis. Personalized at-home neurofeedback compared with long-acting methylphenidate in an european non-inferiority randomized trial in children with adhd. *BMC psychiatry*, 19(1) :237, 2019.
- N. Birbaumer. Clinical-psychological treatment of epileptic seizures : a controlled study. *Perspectives and promises in clinical psychology*, 1991.
- A. Bluschke, F. Broschwitz, S. Kohl, V. Roessner, and C. Beste. The neuronal mechanisms underlying improvement of impulsivity in adhd by theta/beta neurofeedback. *Scientific reports*, 6 :31178, 2016. doi : 10.1038/srep31178.
- A. Bussalbi, M. Congedo, Q. Barthélemy, D. Ojeda, E. Acquaviva, R. Delorme, and L. Mayaud. Clinical and experimental factors influencing the efficacy of neurofeedback in adhd : a meta-analysis. *Frontiers in psychiatry*, 10 :35, 2019.
- F. Catala-Lopez, B. Hutton, A. Núñez-Beltrán, M. J. Page, M. Ridao, D. M. Saint-Gerons, M. A. Catalá, R. Tabarés-Seisdedos, and D. Moher. The pharmacological and non-pharmacological treatment of attention deficit hyperactivity disorder in children and adolescents : a systematic review with network meta-analyses of randomised trials. *PloS one*, 12(7) :e0180355, 2017.
- H. Christiansen, V. Reh, M. H. Schmidt, and W. Rief. Slow cortical potential neurofeedback and self-management training in outpatient care for children with adhd : study protocol and first preliminary results of a randomized controlled trial. *Frontiers in human neuroscience*, 8, 2014. doi : 10.3389/fn-hum.2014.00943.
- J. Cohen. Statistical power analysis for the behavioral sciences 2nd edn. Erlbaum Associates, Hillsdale, 1988.

- S. Cortese, M. Ferrin, D. Brandeis, M. Holtmann, P. Aggensteiner, D. Daley, P. Santosh, E. Simonoff, J. Stevenson, A. Stringaris, et al. Neurofeedback for attention-deficit/hyperactivity disorder : meta-analysis of clinical and neuropsychological outcomes from randomized controlled trials. *Journal of the American Academy of Child & Adolescent Psychiatry*, 55(6) :444–455, 2016. doi : 10.1016/j.jaac.2016.03.007.
- M. Cueli, C. Rodríguez, P. Cabaleiro, T. García, and P. González-Castro. Differential efficacy of neurofeedback in children with adhd presentations. *Journal of clinical medicine*, 8(2) :204, 2019.
- M. Deilami, A. Jahandideh, Y. Kazemnejad, Y. Fakour, S. Alipoor, F. Rabiee, G. S. Pournesaie, R. N. Heidari, and S. A. Mosavi. The effect of neurofeedback therapy on reducing symptoms associated with attention deficit hyperactivity disorder : A case series study. *Basic and clinical neuroscience*, 7(2) :167, 2016. doi : 10.15412/J.BCN.03070211.
- R. Drechsler, M. Straub, M. Doehnert, H. Heinrich, H.-C. Steinhausen, and D. Brandeis. Controlled evaluation of a neurofeedback training of slow cortical potentials in children with attention deficit/hyperactivity disorder (adhd). *Behavioral and brain functions*, 3(1) :35, 2007. doi : 10.1186/1744-9081-3-35.
- N. S. Duric, J. Assmus, D. Gundersen, and I. B. Elgen. Neurofeedback for the treatment of children and adolescents with adhd : a randomized and controlled clinical trial using parental reports. *BMC psychiatry*, 12(1) :107, 2012. doi : 10.1186/1471-244X-12-107.
- S. Enriquez-Geppert, R. J. Huster, and C. S. Herrmann. Eeg-neurofeedback as a tool to modulate cognition and behavior : a review tutorial. *Frontiers in human neuroscience*, 11 :51, 2017. doi : 10.3389/fnhum.2017.00051.
- C. Escolano, M. Navarro-Gil, J. Garcia-Campayo, M. Congedo, and J. Minguez. The effects of individual upper alpha neurofeedback in adhd : an open-label pilot study. *Applied psychophysiology and biofeedback*, 39(3-4) :193–202, 2014. doi : 10.1007/s10484-014-9257-6.
- T. Fuchs, N. Birbaumer, W. Lutzenberger, J. H. Gruzelier, and J. Kaiser. Neurofeedback treatment for attention-deficit/hyperactivity disorder in children : a comparison with methylphenidate. *Applied psychophysiology and biofeedback*, 28(1) :1–12, 2003.
- C. Gani, N. Birbaumer, and U. Strehl. Long term effects after feedback of slow cortical potentials and of theta-beta-amplitudes in children with attention-deficit/hyperactivity disorder (adhd). *Int J Bioelectromagn*, 10(4) :209–232, 2008.

- K. Geladé, T. Janssen, M. Bink, A. Maras, J. Oosterlaan, et al. Behavioral effects of neurofeedback compared to stimulants and physical activity in attention-deficit/hyperactivity disorder : a randomized controlled trial. *The Journal of clinical psychiatry*, 77(10) :e1270–e1277, 2016.
- H. Gevensleben, B. Holl, B. Albrecht, C. Vogel, D. Schlamp, O. Kratz, P. Studer, A. Rothenberger, G. H. Moll, and H. Heinrich. Is neurofeedback an efficacious treatment for adhd? a randomised controlled clinical trial. *Journal of Child Psychology and Psychiatry*, 50(7) :780–789, 2009. doi : 10.1111/j.1469-7610.2008.02033.x.
- H. Heinrich, H. Gevensleben, F. J. Freisleder, G. H. Moll, and A. Rothenberger. Training of slow cortical potentials in attention-deficit/hyperactivity disorder : evidence for positive behavioral and neurophysiological effects. *Biological psychiatry*, 55(7) :772–775, 2004. doi : 10.1016/j.biopsych.2003.11.013.
- H. Heinrich, H. Gevensleben, A. Becker, and A. Rothenberger. Effects of neurofeedback on the dysregulation profile in children with adhd : Scp nf meets sdq-dp—a retrospective analysis. *Psychological medicine*, pages 1–6, 2019.
- M. Holtmann, D. Grasmann, E. Cionek-Szpak, V. Hager, N. Panzner, A. Beyer, F. Poustka, and C. Stadler. Spezifische wirksamkeit von neurofeedback auf die impulsivität bei adhs. *Kindheit und Entwicklung*, 18(2) :95–104, 2009. doi : 10.1026/0942-5403.18.2.95.
- M. Holtmann, B. Pniewski, D. Wachtlin, S. Wörz, and U. Strehl. Neurofeedback in children with attention-deficit/hyperactivity disorder (adhd)—a controlled multicenter study of a non-pharmacological treatment approach. *BMC pediatrics*, 14(1) :202, 2014.
- International Electrotechnical Commission. 60601-2-26 :2012, 2012.
- G. James, D. Witten, T. Hastie, and R. Tibshirani. An introduction to statistical learning. volume 112, chapter 8, pages 303–332. Springer, 2013.
- C. Jeunet, F. Lotte, J.-M. Batail, P. Philip, and J.-A. M. Franchi. Using recent bci literature to deepen our understanding of clinical neurofeedback : A short review. *Neuroscience*, 2018. doi : 10.1016/j.neuroscience.2018.03.013.
- J. D. Kropotov, V. A. Grin-Yatsenko, V. A. Ponomarev, L. S. Chutko, E. A. Yakovenko, and I. S. Nikishena. Erps correlates of eeg relative beta training in adhd children. *International journal of psychophysiology*, 55(1) :23–34, 2005. doi : 10.1016/j.ijpsycho.2004.05.011.

- E.-J. Lee and C.-H. Jung. Additive effects of neurofeedback on the treatment of adhd : A randomized controlled study. *Asian Journal of Psychiatry*, 25 :16–21, 2017. doi : 10.1016/j.ajp.2016.09.002.
- U. Leins, G. Goth, T. Hinterberger, C. Klinger, N. Rumpf, and U. Strehl. Neurofeedback for children with adhd : a comparison of scp and theta/beta protocols. *Applied psychophysiology and biofeedback*, 32(2) :73–88, 2007. doi : 10.1007/s10484-007-9031-0.
- L. Li, L. Yang, C. Zhuo, and Y.-F. Wang. A randomised controlled trial of combined eeg feedback and methylphenidate therapy for the treatment of adhd. *Swiss Med. Wkly*, 143 :w13838, 2013. doi : 10.4414/smw.2013.13838.
- M. Linden, T. Habib, and V. Radojevic. A controlled study of the effects of eeg biofeedback on cognition and behavior of children with attention deficit disorder and learning disabilities. *Applied Psychophysiology and Biofeedback*, 21(1) :35–49, 1996.
- R. Luan, Z. Mu, F. Yue, and S. He. Efficacy and tolerability of different interventions in children and adolescents with attention deficit hyperactivity disorder. *Frontiers in psychiatry*, 8 :229, 2017.
- S. Maurizio, M. D. Liechti, H. Heinrich, L. Jäncke, H.-C. Steinhausen, S. Walitza, D. Brandeis, and R. Drechsler. Comparing tomographic eeg neurofeedback and emg biofeedback in children with attention-deficit/hyperactivity disorder. *Biological psychology*, 95 :31–44, 2014. doi : 10.1016/j.biopsycho.2013.10.008.
- V. Meisel, M. Servera, G. Garcia-Banda, E. Cardo, and I. Moreno. Reprint of “neurofeedback and standard pharmacological intervention in adhd : a randomized controlled trial with six-month follow-up”. *Biological psychology*, 95 : 116–125, 2014. doi : 10.1016/j.biopsycho.2013.09.009.
- J.-A. Micoulaud-Franchi, P. A. Geoffroy, G. Fond, R. Lopez, S. Bioulac, and P. Philip. Eeg neurofeedback treatments in children with adhd : an updated meta-analysis of randomized controlled trials. *Frontiers in human neuroscience*, 8, 2014. doi : 10.3389/fnhum.2014.00906.
- F. Minder, A. Zuberer, D. Brandeis, and R. Drechsler. Informant-related effects of neurofeedback and cognitive training in children with adhd including a waiting control phase : a randomized-controlled trial. *European child & adolescent psychiatry*, pages 1–12, 2018. doi : 10.1007/s00787-018-1116-1.
- A. Mohagheghi, S. Amiri, N. Moghaddasi Bonab, G. Chalabianloo, S. G. Noorazar, S. M. Tabatabaei, and S. Farhang. A randomized trial of comparing the efficacy of two neurofeedback protocols for treatment of clinical and cognitive

- symptoms of adhd : Theta suppression/beta enhancement and theta suppression/alpha enhancement. *BioMed Research International*, 2017, 2017. doi : 10.1155/2017/3513281.
- M. R. Mohammadi, N. Malmir, A. Khaleghi, and M. Aminiorani. Comparison of sensorimotor rhythm (smr) and beta training on selective attention and symptoms in children with attention deficit/hyperactivity disorder (adhd) : A trend report. *Iranian journal of psychiatry*, 10(3) :165, 2015.
- V. J. Monastra, D. M. Monastra, and S. George. The effects of stimulant therapy, eeg biofeedback, and parenting style on the primary symptoms of attention-deficit/hyperactivity disorder. *Applied psychophysiology and biofeedback*, 27(4) :231–249, 2002.
- D. C. Montgomery, E. A. Peck, and G. G. Vining. Introduction to linear regression analysis. volume 821, chapter 5, pages 190–191. John Wiley & Sons, 2012.
- I. Moreno-García, S. Meneres-Sancho, C. Camacho-Vara de Rey, and M. Servera. A randomized controlled trial to examine the posttreatment efficacy of neurofeedback, behavior therapy, and pharmacology on adhd measures. *Journal of attention disorders*, 23(4) :374–383, 2019.
- O. Mowrer. Learning theory and behavior. 1960.
- M. E. Narad, A. A. Garner, J. L. Peugh, L. Tamm, T. N. Antonini, K. M. Kingery, J. O. Simon, and J. N. Epstein. Parent–teacher agreement on adhd symptoms across development. *Psychological assessment*, 27(1) :239, 2015. doi : 10.1037/a0037864.
- G. Ogrim and K. A. Hestad. Effects of neurofeedback versus stimulant medication in attention-deficit/hyperactivity disorder : a randomized pilot study. *Journal of child and adolescent psychopharmacology*, 23(7) :448–457, 2013. doi : 10.1089/cap.2012.0090.
- F. Pedregosa, G. Varoquaux, A. Gramfort, V. Michel, B. Thirion, O. Grisel, M. Blondel, P. Prettenhofer, R. Weiss, V. Dubourg, et al. Scikit-learn : Machine learning in python. *Journal of machine learning research*, 12(Oct) :2825–2830, 2011.
- J. R. Quinlan. Induction of decision trees. *Machine learning*, 1(1) :81–106, 1986.
- S. Rajabi, A. Pakize, and N. Moradi. Effect of combined neurofeedback and game-based cognitive training on the treatment of adhd : A randomized controlled study. *Applied Neuropsychology : Child*, pages 1–13, 2019.

- J. Rogala, K. Jurewicz, K. Paluch, E. Kublik, R. Cetnarski, and A. Wróbel. The do's and don'ts of neurofeedback training : a review of the controlled studies using healthy adults. *Frontiers in human neuroscience*, 10 :301, 2016. doi : 10.3389/fnhum.2016.00301.
- S. Seabold and J. Perktold. Statsmodels : Econometric and statistical modeling with python. In *Proceedings of the 9th Python in Science Conference*, volume 57, page 61. SciPy society Austin, 2010.
- E. Shereena, R. Gupta, C. Bennett, K. Sagar, and J. Rajeswaran. Eeg neurofeedback training in children with attention deficit/hyperactivity disorder : A cognitive and behavioral outcome study. *Clinical EEG and neuroscience*, page 1550059418813034, 2019.
- W. A. Shewhart. *Economic control of quality of manufactured product*. ASQ Quality Press, 1931.
- H. Sollie, B. Larsson, and W.-T. Mørch. Comparison of mother, father, and teacher reports of adhd core symptoms in a sample of child psychiatric outpatients. *Journal of Attention Disorders*, 17(8) :699–710, 2013. doi : 10.1177/1087054711436010.
- E. J. Sonuga-Barke, D. Brandeis, S. Cortese, D. Daley, M. Ferrin, M. Holtmann, J. Stevenson, M. Danckaerts, S. van der Oord, M. Döpfner, R. W. Dittmann, E. Simonoff, A. Zuddas, T. Banaschewski, J. Buitelaar, D. Coghill, C. Hollis, E. Konofal, M. Lecendreux, I. C. Wong, and J. Sergeant. Nonpharmacological interventions for adhd : Systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *American Journal of Psychiatry*, 2013. doi : 10.1176/appi.ajp.2012.12070991.
- N. J. Steiner, R. C. Sheldrick, D. Gotthelf, and E. C. Perrin. Computer-based attention training in the schools for children with attention deficit/hyperactivity disorder : a preliminary trial. *Clinical pediatrics*, 50(7) :615–622, 2011. doi : 10.1177/0009922810397887.
- N. J. Steiner, E. C. Frenette, K. M. Rene, R. T. Brennan, and E. C. Perrin. Neurofeedback and cognitive attention training for children with attention-deficit hyperactivity disorder in schools. *Journal of Developmental & Behavioral Pediatrics*, 35(1) :18–27, 2014. doi : 10.1097/DBP.0000000000000009.
- U. Strehl, U. Leins, G. Goth, C. Klinger, T. Hinterberger, and N. Birbaumer. Self-regulation of slow cortical potentials : a new treatment for children with attention-deficit/hyperactivity disorder. *Pediatrics*, 118(5) :e1530–e1540, 2006. doi : 10.1542/peds.2005-2478.

- U. Strehl, P. Aggensteiner, D. Wachtlin, D. Brandeis, B. Albrecht, M. Arana, C. Bach, T. Banaschewski, T. Bogen, A. Flaig-Rohr, et al. Neurofeedback of slow cortical potentials in children with attention-deficit/hyperactivity disorder : A multicenter randomized trial controlling for unspecific effects. *Frontiers in human neuroscience*, 11, 2017. doi : 10.3389/fnhum.2017.00135.
- K. K. Sudnawa, V. Chirdkiatgumchai, N. Ruangdaraganon, C. Khongkhatithum, U. Udomsubpayakul, S. Jirayucharoensak, and P. Israsena. Effectiveness of neurofeedback versus medication for attention-deficit/hyperactivity disorder. *Pediatrics International*, 60(9) :828–834, 2018.
- R. Tibshirani. Regression shrinkage and selection via the lasso. *Journal of the Royal Statistical Society. Series B (Methodological)*, pages 267–288, 1996.
- M. van Dongen-Boomsma, M. A. Vollebregt, D. Slaats-Willemse, and J. K. Buitelaar. A randomized placebo-controlled trial of electroencephalographic (eeg) neurofeedback in children with attention-deficit/hyperactivity disorder. *J Clin Psychiatry*, 74(8) :821–827, 2013. doi : 10.4088/JCP.12m08321.
- D. Vernon, A. Frick, and J. Gruzelier. Neurofeedback as a treatment for adhd : A methodological review with implications for future research. *Journal of Neurotherapy*, 8(2) :53–82, 2004.
- World Medical Association. *The Declaration of Helsinki 52nd WMA General Assembly*. 2000.



