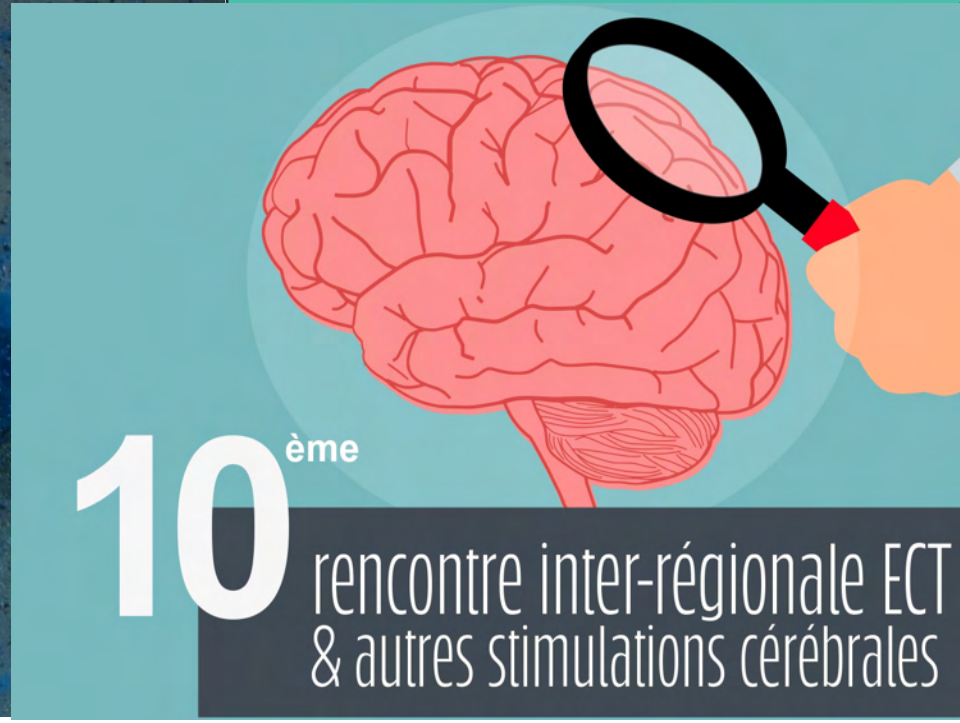


Quel est l'impact de la charge anticholinergique des traitements sur la tolérance cognitive des cures d'ECT chez les patients souffrant d'un épisode dépressif caractérisé ?

Dr Samuel Bulteau (PH) et Dr Andrew Laurin (CCA)

10ème Rencontre Inter-Régionale ECT et autres stimulations cérébrales

1er Juin 2022 – Sotteville-les-Rouens

Conflits d'intérêt

Aucun

Introduction

ECT = traitement non-pharmacologique le plus efficace de la dépression (ultra)résistante [1,2]

ECT = amélioration des troubles cognitifs liés à la dépression [3,4,5] mais …

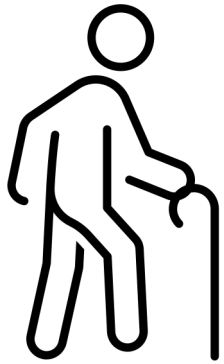
… des effets indésirables cognitifs à court /moyen terme : la mémoire [6,7] (ou dépression ?)

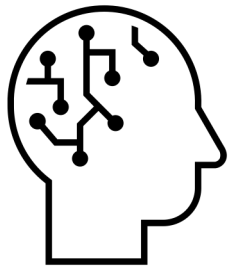
Facteur d'arrêt ou d'appréhension des ECT / ou refus d'une nouvelle cure d'ECT [8]

Enjeux d'optimiser la tolérance cognitive des ECT

→ Plusieurs stratégies possibles [9]

Mais quels impacts des effets anticholinergiques des traitement sur la tolérance cognitive des ECT ?





Les effets anticholinergiques

Anti-muscariniques [10]

Des effets périphériques

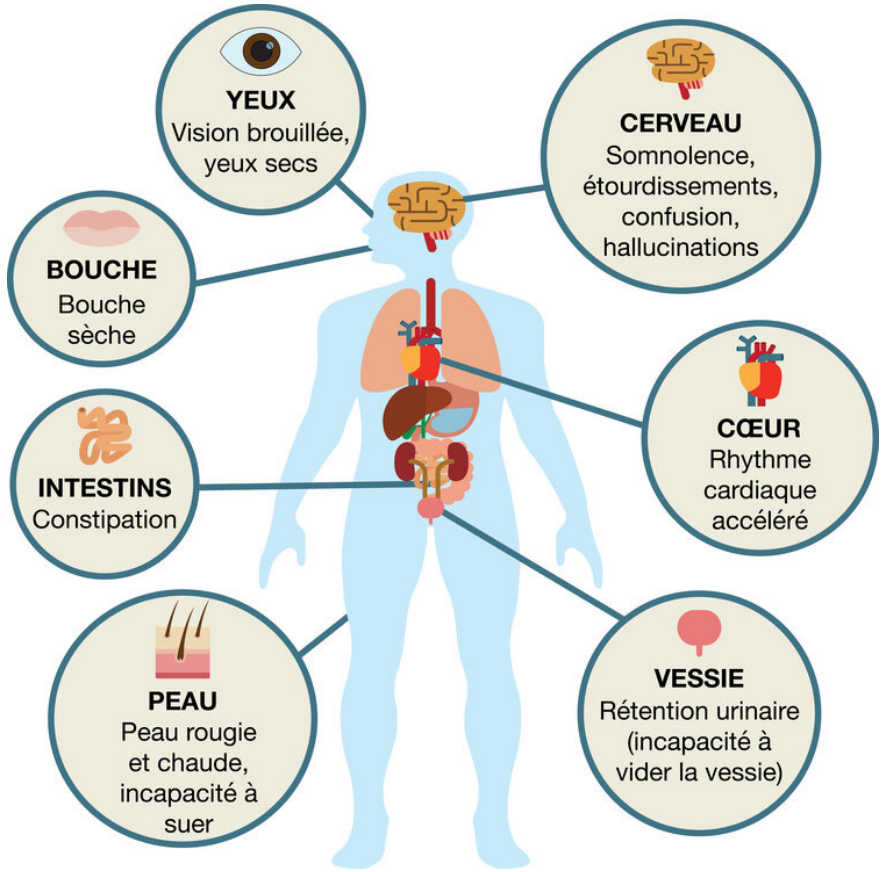
Des effets centraux

Personnes à risque [11,12] :

Personnes âgées

Lésions de la substance blanche

Bas niveau cognitif



- Tricycliques
- Clozapine
- Chlorpromazine
- Cyamemazine
- Hydroxyzine
- Anti-histaminique
- Lepticur
- Parkinan
- Antispasmodique urinaire
- Scopolamine
- Atropine
- *Olanzapine*
- *Quétiapine*

La charge anticholinergique a-t-elle un impact sur la tolérance cognitive des patients souffrant de dépression ?

Journal of Geriatric Psychiatry and Neurology / Vol. 2 / January–March 1989

Glycopyrrolate Versus Atropine in Post-ECT Amnesia in the Elderly

Barbara R. Sommer, MD; Andrew Satlin, MD; Loren Friedman, MS; Jonathan O. Cole, MD

International Clinical Psychopharmacology, 1986, 1, 296–302

Effects of Atropine and Glycopyrrolate on Cognitive Function Following Anaesthesia and Electroconvulsive Therapy (ECT)

B. KELWAY,[1] K. H. SIMPSON,[2] R. J. SMITH[3] and P. J. HALSALL[2]

[1] *Postgraduate School of Psychology, Bradford University, Bradford, U.K.*
[2] *St James's University Hospital, Leeds*
[3] *Department of Psychiatry, University of Leeds*

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Combination of lithium and electroconvulsive therapy (ECT) is associated with higher odds of delirium and cognitive problems in a large national sample across the United States

Rikinkumar S. Patel [a], Anil Bachu [b], Nagy A. Youssef [c, d, e, *]

Méthode

Étude rétrospective monocentrique de dossier

42 patients souffrant d'un EDC uni- ou bipolaire

Recueil des données socio-démo, d'imagerie et d'ECT

MoCA et MADRS avant et après les cures d'ECT (24 à 72h)

Anticholinergic Impregnation Scale (AIS) [13]

Score AIS (AIS cumulé ou △AIS)

ACB (Abilify et la Venlafaxine = 1) [14]

Recueil des traitements quotidien par validation informatique

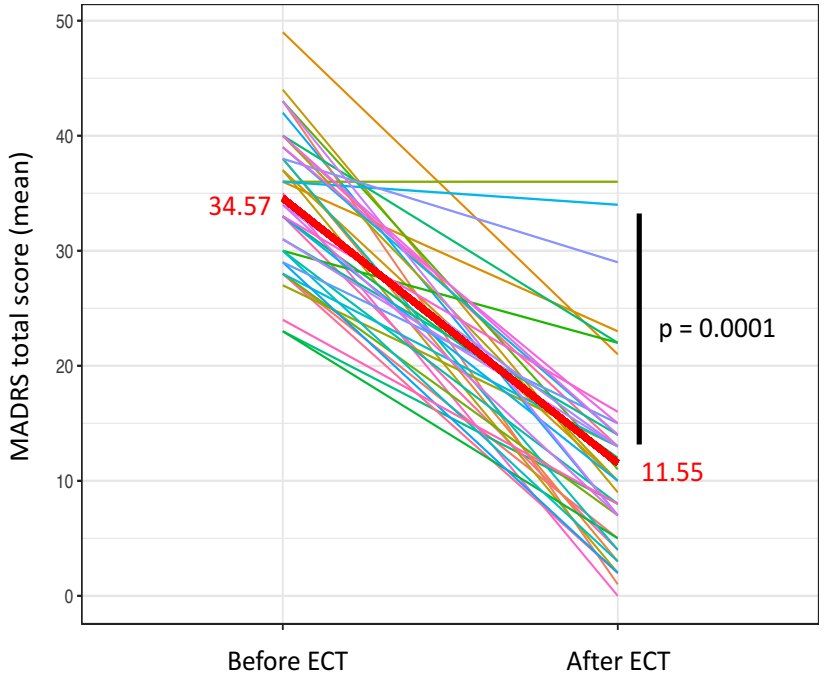
egnation Scale scoring for 128 drugs.

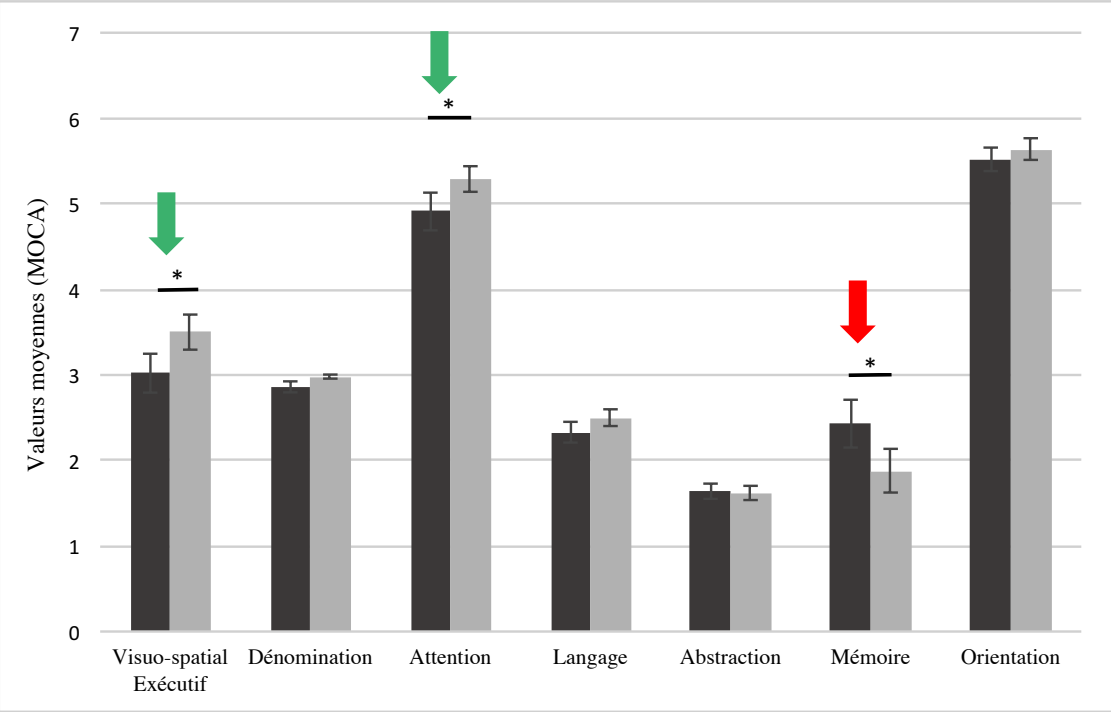
ATC Code	International non-proprietary name	AIS
N06A	Amitriptyline[a,b,c,d]	3
	Amoxapine[c]	3
	Bupropion[c,d]	1
	Citalopram	1
	Clomipramine[b,c]	3
	Dosulepine	2
	Doxepine[c,d]	3
	Duloxetine	1
	Fluoxetine[b,d]	1
	Fluvoxamine[b,c]	1
	Imipramine[a,b,c,d]	3
	Maprotiline	3
	Mirtazapine[a]	1
	Nortriptyline[b,c,d]	
	Paroxetine[d]	
	Phenelzine[b]	
	Sertraline[b,d]	
	Trazodone[a,c,d]	
	Trimipramine	

Résultats

Tableau 1 : Caractéristiques socio-démographiques et cliniques de notre échantillon d'étude (n=42)

	Pré-ECT	Post-ECT	Stat	p-values
Données socio-démographiques :				
Âge (en années)	60.19 ± 14.09	-	-	-
≥ 65 ans	19 (45.24 %)	-	-	-
Sexe (homme)	19 (45.24 %)	-	-	-
Données cliniques :				
Dépression unipolaire	25 (59.52 %)	-	-	-
Dépression bipolaire	17 (40.48 %)	-	-	-
Démence	3 (7.14 %)	-	-	-
MADRS totale	34.57 ± 6.19	11.55 ± 8.39	t = 15.803	**< 0.0001**
MADRS - 50 % (réponse)	-	36 (85.71 %)	-	-
MADRS < 10 (rémission)	-	19 (45.24 %)	-	-
MOCA totale	22.71 ± 4.46	23.41 ± 3.77	t = - 1.323	0.193
MOCA < 26	30 (71.43 %)	28 (66.67 %)	TMN	0.774
AIS totale	4.45 ± 2.29	4.19 ± 2.20	t = 0.848	0.401
AIS > 3	27 (64.29 %)	28 (66.67 %)	TMN	1
AIS cumulée		5.33 ± 2.89	-	-
Données d'imagerie :				
WML aspécifiques	4 (9.52 %)	-	-	-
WML pathologiques	11 (26.19 %)	-	-	-
Atrophie corticale	11 (26.19 %)	-	-	-
Atrophie hippocampique	2 (4.76 %)	-	-	-
Données d'ECT :				
Nombre de séance	-	15.07 ± 4.02	-	-
Charge (en millicoulombs)	-	363.95 ± 167.36	-	-
Durée EEG des crises (en secondes)	-	36.84 ± 14.60	-	-
Placement des életrodes en ULD	-	13 (30.95 %)	-	-
Placement des électrodes en BL	-	29 (69.05 %)	-	-
Changement BL > ULD	-	14 (33.33 %)	-	-
Atropine 0.5 mg injection (> 1 fois)	-	7 (16.67 %)	-	-





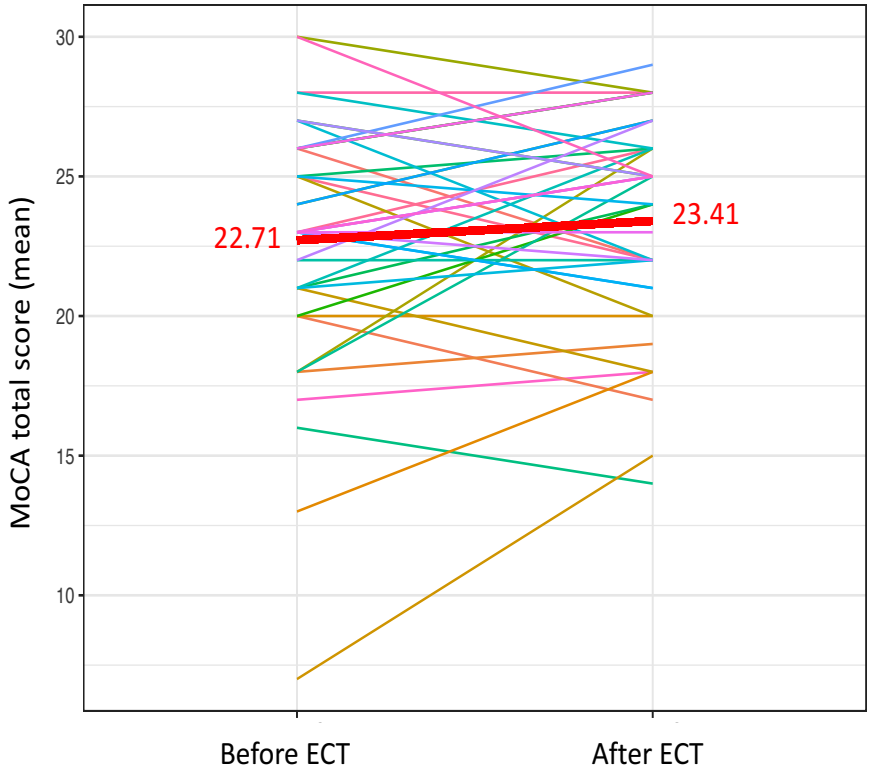
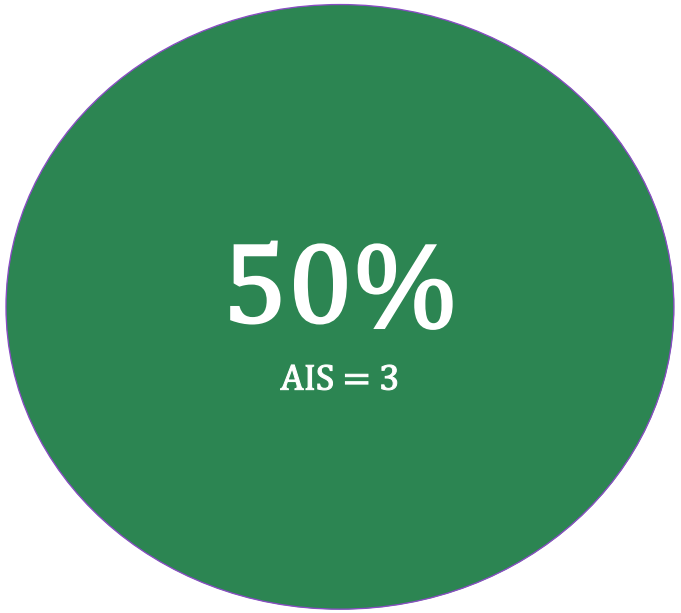


Figure 1 : Évolution des sous-scores de la MOCA avant (en noir) et après (en gris) les cures d'ECT (n=42). Les données correspondent aux valeurs moyennes ± 1 erreur standard. (*) indique une différence statistiquement significative au test t de Student pour les données appariées ($p < 0.05$).

Tableau 4 : Traitements administrés aux patients durant les cures d'ECT (n=42)

Molécule	n	%	Min	Max	Moy	SD	AIS
Lorazepam	20	47.62	0	20	2.98	2.47	1
Venlafaxine	15	35.71	0	262,5	134.49	78.03	1*
Cyamemazine	11	26.19	0	325	44.35	35.37	3
Clomipramine	10	23.81	0	225	84.40	46.57	3
Quetiapine	9	21.43	0	1200	383.96	225.06	2
Mirtazapine	8	19.05	0	60	24.53	11.44	1
Oxazepam	8	19.05	0	150	34.67	19.25	1
Olanzapine	8	19.05	0	15	8.66	3.92	2
Lithium LP	7	16.67	0	1400	655.02	277.87	1
Loxapine	7	16.67	0	400	67.27	55.28	2
Aripiprazol	6	14.29	0	20	9.75	4.31	1*
Diazepam	6	14.29	0	60	15.61	6.51	1
Alimémazine	3	7.14	0	20	13.28	3.80	1
Fluoxetine	3	7.14	0	40	21.70	6.00	1
Pramipexol	3	7.14	0	3.15	1.12	0.36	1
Alprazolam	2	4.76	0	0.50	0.20	0.04	1
Amitriptiline	2	4.76	0	150	114.69	32.29	3
Levodopa	2	4.76	125	400	361.70	78.10	1
Tramadol	2	4.76	0	100	14.55	3.47	1
Atenolol	1	2.38	0	50	44.35	-	1
Baclofène	1	2.38	0	40	34.89	-	1
Cetirizine	1	2.38	0	5	1.28	-	2
Chlortalidone	1	2.38	0	12.5	11.09	-	1
Citalopram	1	2.38	0	40	21.61	-	1
Clorazepate	1	2.38	30	40	38.33	-	1
Duloxetine	1	2.38	0	90	38.91	-	1
Hydroxyzine	1	2.38	0	50	8.14	-	3
Levomepromazine	1	2.38	0	250	101.02	-	2
Risperidone	1	2.38	0	3	1.63	-	1
Sodium valpromide	1	2.38	0	1200	620.34	-	1

Les données sont exprimées en effectif et %, Min : dose minimale quotidienne, Max : dose maximum quotidienne, Moy : dose moyenne quotidienne reçues durant les cures d'ECT en milligrammes / jour, SD : standard déviation, AIS : score anticholinergique de l'Anticholinergic Impregnation Scale (* indique une charge anticholinergique selon l'Anticholinergic Cognitive Burden scale).



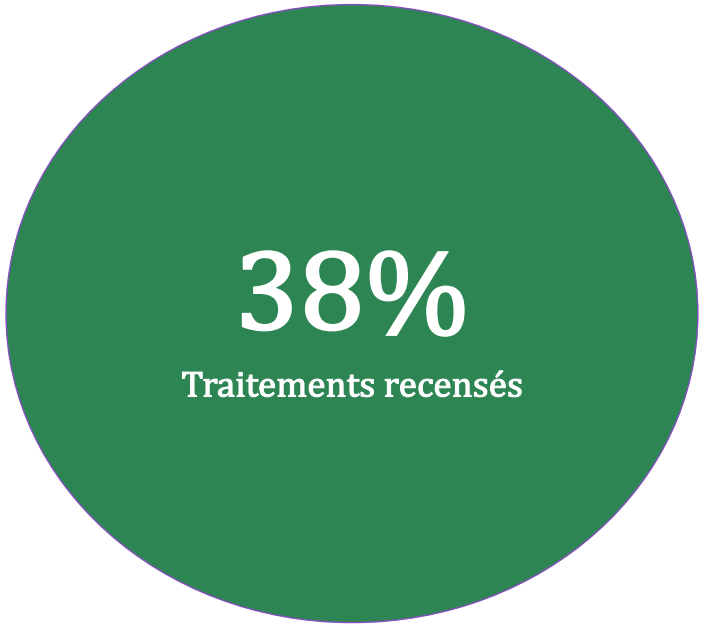


Table 4: Association between cumulated AIS and reduction in MOCA scores with results adjusted for ΔMADRS using logistic regression

	Adjusted OR	95% CI lower	95% CI upper	p-values
MOCA total score	1.038	0.984	1.095	0.175
Visuo-executive	0.981	0.934	1.029	0.430
Attention	1.005	0.965	1.047	0.800
Language	0.989	0.947	1.032	0.601
Abstraction	0.973	0.932	1.015	0.208
Delayed recall	0.972	0.922	1.025	0.295
Orientation	1.000	0.961	1.042	0.983

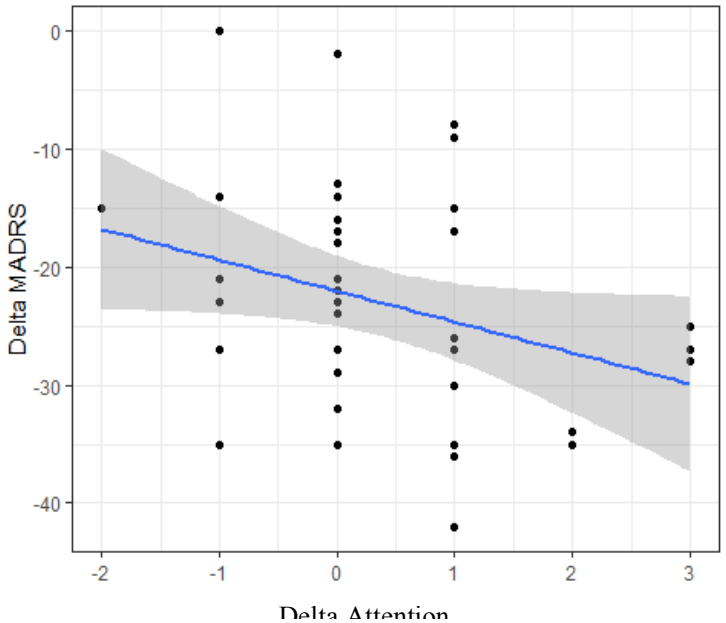


Table 5: Association between ΔAIS and reduction in MOCA scores with results adjusted for ΔMADRS using logistic regression

	Adjusted OR	95% CI lower	95% CI upper	p-values
MOCA total score	1.015	0.939	1.098	0.706
Visuo-executive	0.997	0.930	1.069	0.936
Attention	0.991	0.935	1.051	0.771
Language	1.020	0.960	1.085	0.522
Abstraction	1.011	0.950	1.076	0.727
Delayed recall	0.982	0.910	1.061	0.653
Orientation	0.968	0.914	1.025	0.270

Discussion

Première étude sur le sujet en incluant une analyse sur tous les traitements reçus lors des ECT

Condition naturaliste

La charge anticholinergique n'est pas un facteur de mauvais pronostic de la tolérance cognitive des ECT

Hypothèse initiale non confirmée

Plusieurs explications possibles :

- Effets pro-cognitifs des ECT > aux effets anticholinergique ?
- Taille limite de l'échantillon
- La limite des échelles d'évaluation ?

ECHELLES ANTICHOLINERGIQUES [15,16,17,18,19]
Les interactions pharmacologiques
La durée de prescription
Les comorbidités
L'homogénéité des valeurs anticholinergiques
Fonctions rénales et hépatiques
L'absence de prise en compte de l'affinité des molécules
Traitements non recensés (600 in vivo)

EVALUATION COGNITIVE
L'évaluation cognitive avec la MoCA
Vers l'utilisation de nouveaux d'outils spécifique à l'ECT ?

SAA

Limites

ELECTROCONVULSIVE COGNITIVE ASSESMENT

ECCA

<10 min, possible en distanciel

Patient's Name _____ ECT Type ____ # ____

Age ____ DOB ____ / ____ / ____ Years of Education # ____

Evaluator's Name _____ Date ____ / ____ / ____

ORIENTATION

points ___ /4

Year [ ] Month [ ] Date [ ] Place [ ]

SUBJECTIVE

Answer Yes or No. Give the point if the answer is negative.

___ /4

1. [Y] [N] Are you having difficulty with your memory?
2. [Y] [N] Are you feeling confused now?
3. [Y] [N] Are you having difficulty paying attention to things that go on around you?
4. [Y] [N] Are you having difficulty remembering movies/TV shows that you have recently seen?

INFORMANT

Name _____ Relationship _____

___ /4

Give the point if the answer is negative

1. [Y] [N] Is the patient having difficulty with his/her memory?
2. [Y] [N] Is the patient having difficulty following a conversation?
3. [Y] [N] Is the patient having difficulty remembering events that happened more than a year ago?
4. [Y] [N] Is the patient having difficulty remembering events that happened during the past week?

REGISTRATION

Read the list twice. Inform the subject that they will need to recall the words later on.

PRE ECT	[ ] Home	[ ] Army	[ ] Picture	[ ] Green
Mid ECT	[ ] House	[ ] Queen	[ ] Corner	[ ] Red
POST ECT	[ ] Dress	[ ] King	[ ] Engine	[ ] Blue

*
*

ATTENTION

___ /3

PRE ECT	MID ECT	POST ECT
1. [ ] Serial sevens ***(start at 100)*** 93 86 79 72 65	1. [ ] Serial sevens ***(start at 90)*** 83 76 69 62 55	1. [ ] Serial sevens ***(start at 80)*** 73 66 59 52 45
2. [ ] Trail B 1A 2B 3C 4D 5E 6F 7G 8H 9I 10J	2. [ ] Trail B 5E 6F 7G 8H 9I 10J 11K 12L 13M 14N	2. [ ] Trail B 10J 11K 12L 13M 14N 15O 16P 17Q 18R 19S
3. [ ] Months Backwards D N O S A J J M A M F J	3. [ ] Months Backwards S A J J M A M F J D N O	3. [ ] Months Backwards J J M A M F J D N O S A

AUTOBIOGRAPHICAL MEMORY

(Corroborate with informant. Write the answers.)

___ /6

1. [ ] Recall where he/she went on the last overnight trip
2. [ ] Recall what he /she did last New Year's Eve
3. [ ] Recall what he or she did on his/her last birthday
4. [ ] Recall what he /she had for dinner the night before
5. [ ] Recall what was the last restaurant he/she visited
6. [ ] Recall what psychiatric medications he/she is taking

FACTUAL KNOWLEDGE

___ /5

1. [ ] What are the colors of the flag?
2. [ ] Who was the previous president/prime minister?
3. [ ] What is the capital of your state/province?
4. [ ] How many days are in a year?
5. [ ] How many states/provinces are in your country?_____

RECALL

___ /4

PRE ECT	[ ] Home	[ ] Army	[ ] Picture	[ ] Green
MID ECT	[ ] House	[ ] Queen	[ ] Corner	[ ] Red
POST ECT	[ ] Dress	[ ] King	[ ] Engine	[ ] Blue

Depression Scale Baseline _____ Current _____

TOTAL ____ / 30

Journal of Affective Disorders Volume 269, 15 May 2020, Pages 36-42

19

Au final : quelles implications en pratique ?

- Ne pas limiter la prescription de psychotropes utiles pour les patients par crainte d'une moins bonne tolérance cognitive des ECT
- Sauf prudence accrue sur les terrains à risque comme les personnes âgées ou les bas niveaux cognitifs qui vont bénéficier d'ECT : balance bénéfice / risque ? → surveillance accrue de la tolérance cognitive (indépendamment des ECT finalement) mais aussi de la charge anticholinergique
- Le besoin d'améliorer les échelles d'évaluation des scores anticholinergiques

→ http://www.acbcalc.com/

1. UK ECT Review Group, 2003. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet 361 (9360), 799–808.

2. CANMAT Depression Work Group, 2016. Canadian network for mood and anxiety treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 4. Neurostimulation treatments. Can. J. Psychiatr. Revue Canadienne De Psychiatrie 61 (9), 561–575.

3. Vann Jones, S., McCollum, R., 2019. Subjective memory complaints after electroconvulsive therapy: systematic review. BJPsych Bull. 43 (2), 73–80.

4. Porter, et al. 2020. Cognitive side-effects of electroconvulsive therapy: what are they, how to monitor them and what to tell patients. BJPsych Open 6 (3), e40.

5. Hebbrecht et al. 2020. Cognitive change after electroconvulsive therapy in mood disorders measured with the Montreal Cognitive Assessment. Acta Psychiatr. Scand. 142 (5), 413–422.

6. Basso et al. 2020. Antidepressant and neurocognitive effects of serial ketamine administration versus ECT in depressed patients. J. Psychiatr. Res. 123, 1–8.

7. Semkovska, M., McLoughlin, D.M., 2013. Measuring retrograde autobiographical amnesia following electroconvulsive therapy: historical perspective and current issues. J. ECT 29 (2), 127–133.

8. Sienaert, P.A., Vansteelandt, K., Demyttenaere, K., Peuskens, J., 2010. Predictors of patient satisfaction after ultrabrief bifrontal and unilateral electroconvulsive therapies for major depression. J. ECT 26 (1), 55–59.

9. Mankad, M.V., Beyer, J.L., Weiner, R.D., Krystal, A., 2010. Clinical Manual of Electroconvulsive Therapy. American Psychiatric Publishing, Inc.

10. Nishtala, P.S., Salahudeen, M.S., Hilmer, S.N., 2016. Anticholinergics: theoretical and clinical overview. Expet Opin. Drug Saf. 15 (6), 753–768.

11. Lo´pez-A´lvarez, J., Sevilla-Llewellyn-Jones, J., Agüera-Ortiz, L., 2019. Anticholinergic drugs in geriatric psychopharmacology. Front. Neurosci. 13, 1309.

12. Oudega et al. 2014. White matter hyperintensities and cognitive impairment during electroconvulsive therapy in severely depressed elderly patients. Am. J. Geriatr. Psychiatr. 22 (2), 157–166.

13. Briet et al. 2017. The anticholinergic impregnation scale: towards the elaboration of a scale adapted to prescriptions in French psychiatric settings. Therapie 72 (4), 427–437.

14. Campanelli, C.M., 2012. American Geriatrics Society 2012 Beers criteria update expert panel American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. J. Am. Geriatr. Soc. 60 (4), 616–631.

15. Sathienluckana et al. 2018. Anticholinergic discontinuation and cognitive functions in patients with schizophrenia: a pharmacist-physician collaboration in the outpatient department. Integrated Pharm. Res. Pract. 7, 161–171.

16. Bishara et al. 2017. Anticholinergic effect on cognition (AEC) of drugs commonly used in older people: anticholinergic effect on cognition. Int. J. Geriatr. Psychiatr. 32 (6), 650–656. https://doi.org/10.1002/ gps.4507.

17. Fox et al. 2011. Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study: anticholinergic activity and cognition. J. Am. Geriatr. Soc. 59 (8), 1477–1483.

18. Ruxton, K., Woodman, R.J., Mangoni, A.A., 2015. Drugs with anticholinergic effects and cognitive impairment, falls and all-cause mortality in older adults: a systematic review and meta-analysis: anticholinergics and adverse outcomes in older adults. Br. J. Clin. Pharmacol. 80 (2), 209–220.

19. Zarowitz, B.J., 2006. Oral solid potassium chloride and anticholinergic medications: a new drug interaction for an old drug? Geriatr. Nurs. 27 (6), 329–333.

Merci de votre attention !

Des questions ?