Journal of Affective Disorders 188 (2015) 47–52

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Cognitive and psychomotor effects of three months of escitalopram treatment in elderly patients with major depressive disorder

Lieve Lia Beheydt [a,b,*], Didier Schrijvers [a,b], Lise Docx [a,c], Filip Bouckaert [d], Wouter Hulstijn [a], Bernard Sabbe [a,b]

[a] Collaborative Antwerp Psychiatric Research Institute (CAPRI), Antwerp University, Antwerp, Belgium
[b] University Psychiatry Center, Psychiatric Hospital, Duffel, Belgium
[c] Psychiatric Hospital, Broeders Alexianen, Boechout, Belgium
[d] University Psychiatric Center KU Leuven, Kortenberg, Belgium

ARTICLE INFO

Article history:
Received 3 June 2015
Received in revised form
14 August 2015
Accepted 18 August 2015
Available online 28 August 2015

Keywords:
Major depression
Elderly
Psychomotor retardation
Cognitive
Escitalopram
Functional burden

ABSTRACT

Background: Although psychomotor retardation (PR) and cognitive disfunctioning are essential symptoms of elderly depressed patients, the differential effect of treatment with an SSRI in the elderly on these symptoms has hardly got any attention in studies with objective experimental measures. Since effects appear relatively slower in elderly, this study evaluates the effect on cognitive and psychomotor functioning as compared to mood, on four points during a twelve week follow up of monotreatment with escitalopram.

Method: 28 non-demented elderly unipolar depressive patients on 5–20 mg escitalopram were compared to 20 matched healthy elderly. All participants underwent a test battery containing clinical depression measures, cognitive measures of processing speed, executive function and memory, clinical ratings of PR, and objective computerized fine motor skill-tests at the start and after 2, 6 and 12 weeks. Statistical analysis consisted of a General Linear Model (GLM) repeated measures multivariate analysis of variance of completers to compare the psychomotor and cognitive outcomes of the two groups.

Results: Although, apart from the significant mood effect, no interaction effects were found for the psychomotor and cognitive tasks, the means in general show a trend of differential effects in cognitive and psychomotor functions, with smaller effects and delayed timeframes and with presence of subgroups compared to mood effects.

Limitation: Longer follow up studies are necessary to evaluate differential long term effects.

Conclusion: In elderly, moderate effects of SSRI treatment on mood precede slow or limited effects on cognition and psychomotor retardation.

1. Introduction

Selective Serotonin Reuptake Inhibitors (SSRIs), and especially escitalopram and sertraline appear to be the first choice antidepressant pharmacological treatment for Major Depressive Disorder (MDD) (Cipriani et al., 2009), given their favorable balance between benefits (Cipriani et al., 2009; Kok et al., 2012), tolerability (Kasper et al., 2005; Mao et al., 2008; Gorwood et al., 2007; Bose, Li and Gandhi, 2008), and acquisition cost.

Psychomotor symptoms have clinical relevance and they are indicative of melancholic depression with or without psychotic features, and could be relevant in the choice of antidepressants (Schrijvers et al., 2008). In psychomotor functioning, three domains are generally distinguished: fine versus gross motor functioning, and speech functioning (Bennabi et al., 2013; Buyukdura et al., 2011; Schrijvers et al., 2008; Sobin and Sackeim, 1997).

Despite the importance of the psychomotor symptom cluster and the widespread use of SSRIs in the treatment of MDD, only few studies have investigated the impact of SSRIs on Psychomotor Retardation (PR). Some of these studies applied subjective observer-rated methods such as the retardation item of the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960) and the Salpêtrière Retardation Rating Scale (SRRS) (Widlöcher and Ghozlan, 1989), whereas very few used an objective measurement method (Greden and Carroll, 1981), a battery of figure copying tasks with the use of a pressure-sensitive pen and a digitizer. The latter technique results in objective and real-time recordings of perceptual motor activity and enables to distinguish between the cognitive and motor processes involved in a writing movement.

* Correspondence to: Medical and Health Science Department, Collaborative Antwerp Psychiatric Research Institute (CAPRI), Antwerp University, Campus Drie Eiken – gebouw R D.R.328, Universiteitsplein 1, Antwerp 2610, Belgium.
E-mail address: lieve.beheydt@uantwerpen.be (L.L. Beheydt).

http://dx.doi.org/10.1016/j.jad.2015.08.041
0165-0327/

Hegerl et al. (2005) and Mergl et al. (2004) reported an increase in velocity of rapid hand movements after treatment with [reboxetine and] citalopram, applying such a computerized test battery during a 4-week treatment. Sabbe et al. (1996) treated depressed inpatients, for whom other psychotropic medication was restricted to the absolute minimum, during six weeks with fluoxetine 20 mg and observed an overall cognitive but no motor improvement on a battery of digitized writing tasks. Using the same drawing tasks, Schrijvers et al. (2009) compared the psychomotor performance of 22 MDD inpatients to a control group of 19 healthy subjects to evaluate during 6 weeks the effect of treatment with 50 mg sertraline, while ruling out effects of other psychotropic medication. They found decreased cognitive and motor times in patients for copying simple lines or figures, but no decrease in motor times for drawing more complex figures, with a higher cognitive load for motor planning.

Depression presents differently in elderly, with less mood complaints and more somatic, psychomotor and cognitive symptoms (Alexopoulos et al., 2002). Moreover, depression may be secondary to a different medical condition or drug, entailing more risk of drug–drug and drug-disease interaction and adverse effects of medication. In addition, aging itself causes decline in psychomotor and cognitive functioning (Alexopoulos et al., 2002). PR is a particularly relevant symptom cluster, given its direct relationship with loss of activity and functioning in daily life (Santos et al., 2012), reduced self-care, and higher risk of falling (Chen et al., 2012). It would even be bi-directionally associated as a risk-factor for and as a result of depression. Moreover, PR is more distinct in elderly (Parker et al., 2000, 2001), and characteristic for the dysexecutive syndrome (Lockwood et al., 2002). Finally, PR predicts poor treatment response and chronicity of geriatric depression (Kalayam and Alexopoulos, 1999).

SSRIs are efficacious, but elicit a delayed response in depression in elderly, compared to younger patients (Kok et al., 2012; Topiwala et al., 2014). In the very old, SSRIs are more effective than placebo, but only in severe depression. Important differences in results were found with ranges of 18 to 82% for placebo and 16 to 80% for citalopram (Roose et al., 2004). Finally, SSRI reduces the relapse rate significantly (Gorwood et al., 2007), known to be higher in elderly patients (Mitchell and Subramaniam, 2005).

Non-responders to SSRIs appear to be a subgroup with standard cognitive impairments (Culang et al., 2009). Citalopram-treated patients with deficient response inhibition show an even worse response than placebo-treated patients. With intact response inhibition, on the contrary, results are the reverse (Sneed et al., 2010).

This study will investigate the differential effects of escitalopram on cognitive and psychomotor measures in elderly patients and compare them to mood effects, without interfering effects of other psychotropic medication. Since effects of SSRIs in elderly are slower, the timeframes of the various symptoms were also compared. Drawing on previous research, we hypothesize, apart from a decrease in depressive symptoms, a decrease of motor time in simple motor tasks (Hegerl et al., 2005; Mergl et al., 2004), an improvement of all cognitive measures and of cognitive initiation times (Sabbe et al., 1996), but no improvement of motor times in complex motor tasks involving more motor planning (Schrijvers et al., 2009). Further, we explore the possibility of the existence of subgroups in elderly patients, based on processing speed.

2. Materials and methods

For a full description of the study population, inclusion and exclusion criteria, assessments and tasks and baseline results, see the baseline report of this investigation (Beheydt et al., 2015).

Twenty-eight non-demented (Mini Mental State Examination (MMSE) Score >24) elderly (age >60) medication-free in- and outpatients with unipolar single episode or recurrent MDD (score on Geriatric Depression Scale (GDS) >11; Yesavage and Brink, 1982) were compared to 20 healthy controls, matched for age, gender, education and vascular risks.

All participants were administered a questionnaire about health, medication, wellbeing status and educational level. Next, the MMSE (Kok and Verhey, 2002) and GDS were administered. After inclusion, the cognitive and psychomotor functioning of this group were compared to those of the healthy elderly at four time points (T) after the start of treatment with escitalopram 5–20 mg: at baseline and at week two, six and twelve. All assessments took place in the afternoon.

Clinical depression severity was assessed using the GDS (30 items) (Yesavage and Brink, 1982), whereas the State and Trait Anxiety Inventory (STAI 1, STAI2) (Spielberger et al., 1983) informed about the degree of anxiety symptoms. The 15-item Salpêtrière Retardation Rating Scale (SRRS) (Widlöcher and Ghozlan, 1989) was administered to assess the clinical level of psychomotor retardation.

For the objective psychomotor assessment, participants were asked to copy lines (CL) or figures (CF) from a computer screen with the use of a special pressure-sensitive pen and a digitizer (Maarse et al., 1988). The initiation time (IT), the time between the presentation of the stimulus and the start of the first drawing movement, and the motor time (MT), the time from the start of the first drawing movement to the end of the last drawing movement, were calculated. In the second task, the reinspection time (REIN T), the time from retouching the starting spot to resuming starting the drawing, was also determined. Reinspection time was not included in the motor time. For the Symbol Digit Substitution Test (SDST) (Mc Leod et al., 1982), the same recording techniques were used as with the copying tasks. The following variables were analyzed: the number of correct answers (SDST NCORR), the matching time, i.e., initiation time (SDST IT), and the writing time, i.e., motor time (SDST MT).

Cognitive functioning was assessed using the computerized Wisconsin Card Sorting Test (WCST; Barceló and Knight, 2002; Greve et al., 2002). Indices used were the number of correct answers (WCST NCORR) and the number of categories (WCST CAT) completed. Additionally, from the Stroop color-word test (Mc Leod, 1991) the variables reading speed (Stroop1) and interference (Stroop INT) were analyzed. From the 15-words verbal memory test (Saan and Deelman, 1986), only the number of correct recalls in the fifth trial (15W TOT) was recorded (Verbal Memory Total). The delayed recall was scored as 15W RECALL. For the Verbal Memory Recognition too, only correct recognitions (15W RECOG) were scored.

Statistical analysis of the data was performed using SPSS 17.00. and consisted of a General Linear Model (GLM) repeated measures completers analysis to compare the psychomotor and cognitive outcomes of the two groups on all assessment moments, with Time as within-subjects factor and Group as between-subjects factor (Field, 2009). When sphericity could not be assumed, the Greenhouse Geisser correction was used to reduce Type 1 errors. Effect sizes were calculated with partial η^2. Completers analysis was chosen because of the known high variance between and within patients, which makes estimations inappropriate. However, in order to rule out completers bias, the power could be improved by a Last Observation Carried Forward (Supplement Table 3), because drop out patients never got better afterwards and the risk of Type 1 errors was non-existent. The LOCF was only used to check the reliability of the data found in the completers group (Supplement Table 1). Subsequently, an exploratory analysis tested for differences between patients with high (<28) and low level

(≥ 28) processing speed, using the median as a (central tendency) cut off score between the groups.

3. Results

After screening 41 patients for severe comorbidity, dementia and cardiovascular contra-indications, 28 patients were included. Subsequently, 11 patients and 1 control fell out because of unexpected medical or functional adverse events, leaving 17 patients and 20 controls in the end (Supplement Fig. 1). Drop out patients only differed in gender, with more female drop outs.

There were no significant differences between groups on demographic variables. Patients were significantly more depressed ($F(1,34)=112.58$; $p<0.001$), more anxious ($F(1,34)=25.32$; $p<0.001$) and showed more psychomotor retardation (SSRS) ($F(1,34)=33.77$; $p<0.001$) and cognitive impairment (MMSE) ($F(1,34)=7.48$; $p=0.001$) at baseline assessment (Table 1).

Following treatment with escitalopram, patients showed a significant response, but no remission (GDS > 11). Also, the anxiety scale of patients decreased significantly. The SRRS, showed no significant time effect in patients, likely due to the high variance ($1.876 < SEM < 2.899$). Interaction effects were restricted to depression and anxiety, whereas both group effects and learning effects were found for motor times and processing speed. Cognitive measures and cognitive initiation times, on the other hand, only showed differences between groups (see Table 2). In the cognitive and psychomotor variables, no significant interaction effect of time and group was found. However, all variables, except the memory tests and the SDSTIT, showed significant group differences, favoring the control group. Anxiety, processing speed, memory tasks and psychomotor measures showed a positive evolution over time for both groups, probably due to learning effects. These effects were not found in SSRS, SDSTIT, Stroop and WCST measures. Although no significant interaction effect was found (Table 2), scrutinizing the means (Table 1) suggests more subtle and delayed effects for psychomotor and cognitive variables. Yet, after sorting the patients in a high (H) and a low group (L) of processing speed, the high-group did not differ significantly from the control group in cognitive and psychomotor variables, except in WCST NCORR ($F(120)=15.55$, $p=0.001$), whereas the low group did, except in memory measures (Fig. 1).

4. Discussion

The results of this study can be summarized in four points. The main conclusion is that, while a treatment of 12 weeks with escitalopram improves mood to a moderate level, cognitive and fine motor functioning change much less over a same period.

Further, detailed analyses indicated different timeframes and stagings of change, which suggest slowed and delayed change. Even mood symptoms did not reach remission (GDS > 11). Scrutinizing the means showed that interaction effects do exist, attenuated, however, by the typical large variance of populations of higher age. Given the slower and delayed change in symptoms, longer follow up research in elderly would seem indicated.

Also, two subtypes of patients emerged, differing on cognitive

Table 1
Means (and standard deviations) of cognitive and psychomotor assessment scores at baseline and at week 2, 6 and 12 suggest differentiated time frames and stagings of change.

	Number	Week 0 mean (sd)	Week 2 mean (sd)	Week 6 mean (sd)	Week 12 mean (sd)
GDS patient	16	17.69 (4.69)	16.44 (4.43)	12.25 (5.41)	11.63 (6.03)
GDS control	18	4.33 (2.56)	4.33 (2.35)	3.94 (2.56)	3.56 (2.62)
STAI 1 patient	16	50.94 (11.29)	50.31 (8.72)	44.81 (9.85)	44.06 (11.68)
STAI 1 control	19	34.84 (7.89)	32.16 (6.25)	33.53 (6.74)	31.53 (6.81)
SRRS patient	17	15.13 (8.79)	15.19 (7.26)	13.00 (10.03)	10.88 (9.54)
SRRS control		/	/	/	/
SDST patient	13	29.15 (11.68)	30.92 (11.54)	31.85 (12.50)	36.08 (14.68)
SDST control	17	43.35 (9.25)	45.53 (9.33)	46.18 (8.86)	47.71 (10.32)
Stroop 1 patient	14	55.86 (11.07)	58.21 (11.92)	56.57 (12.57)	57.14 (11.43)
Stroop 1 control	18	47.00 (11.45)	47.33 (9.20)	46.00 (7.07)	47.00 (7.83)
Stroop INT patient	13	99.85 (98.55)	74.23 (53.19)	71.31 (53.67)	69.77 (66.98)
Stroop INT control	18	45.83 (22.09)	41.06 (24.94)	39.11 (23.45)	34.67 (17.52)
WCST CAT patient	11	0.45 (0.82)	0.64 (1.03)	0.91 (1.2)	0.91 (1.58)
WCST CAT control	15	2.07 (1.03)	1.47 (0.83)	1.80 (0.86)	1.93 (1.10)
WCST NCORR patient	10	30.40 (12.42)	27.50 (9.89)	28.00 (6.90)	37.70 (10.48)
WCST NCORR control	15	38.67 (9.36)	38.60 (9.09)	40.07 (6.41)	40.60 (7.94)
15W TOT patient	16	7.81 (2.88)	9.56 (3.35)	8.62 (3.44)	9.75 (3.13)
15W TOT control	18	9.5 (2.62)	10.72 (2.76)	10.11 (2.89)	10.28 (2.68)
15W RECALL patient	16	5.25 (3.51)	7.19 (4.28)	6.88 (4.32)	6.81 (3.71)
15W RECALL control	18	6.61 (3.15)	7.17 (2.62)	8.44 (2.66)	7.56 (2.83)
15W RECOG patient	14	23.14 (4.26)	24.86 (5.02)	24.79 (4.17)	25.93 (3.45)
15W RECOG control	17	25.59 (2.62)	26.71 (2.85)	26.00 (2.94)	26.29 (2.76)
CL IT patient	13	1.28 (0.28)	1.15 (0.19)	1.06 (0.22)	1.07 (0.22)
CL IT control	19	0.97 (0.17)	0.93 (0.17)	0.86 (0.14)	0.86 (0.15)
CL MT patient	13	0.69 (0.26)	0.60 (0.22)	0.56 (0.23)	0.54 (0.20)
CL MT control	19	0.49 (0.17)	0.40 (0.13)	0.36 (0.11)	0.36 (0.11)
FC IT patient	12	2.72 (0.50)	2.79 (0.42)	2.68 (0.73)	2.48 (0.58)
FC IT control	19	2.50 (0.78)	2.30 (0.37)	2.25 (0.31)	2.21 (0.35)
FC MT patient	13	3.19 (1.56)	2.65 (1.17)	2.70 (1.81)	2.75 (1.80)
FC MT control	19	2.08 (0.71)	1.89 (0.52)	1.83 (0.47)	1.86 (0.46)
FC ReinT patient	13	0.23 (0.56)	0.18 (0.32)	0.21 (0.61)	0.29 (0.80)
FC ReinT control	19	0.01 (0.04)	0.06 (0.11)	0.02 (0.01)	0.02 (0.05)
SDST IT patient	9	2.50 (1.70)	2.10 (0.94)	1.92 (1.04)	1.89 (0.94)
SDST IT control	17	1.48 (0.46)	1.37 (0.44)	1.33 (0.37)	1.21 (0.44)
SDST MT patient	9	0.77 (0.22)	0.79 (0.20)	0.81 (0.25)	0.77 (0.18)
SDST MT control	17	0.66 (0.13)	0.64 (0.11)	0.66 (0.16)	0.73 (0.19)

Table 2
Only depression and anxiety show interaction effects. Motor times and processing speed show group effects as well as learning effects. Cognitive measures AND cognitive initiation times ONLY show differences between groups.

Measure	df	*F*	*p*	η^2
GDS				
Time	(3, 74.385)	14.522	< 0.001**	0.312
Time*Group	(3, 74.385)	9.188	< 0.001**	0.223
Group	(1, 32)	84.159	< 0.001**	0.725
STAI I				
Time	(2.474, 81.634)	5.859	0.001**	0.151
Time*Group	(2.474, 81.634)	2.912	0.049*	0.081
Group	(1, 33)	34.187	< 0.001**	0.509
SSRS				
Time (patients only)	(3, 45)	0.265	0.850	0.017
WTOT				
Time	(3, 96)	5.948	0.001**	0.157
Time*Group	(3, 96)	0.821	0.485	0.025
Group	(1, 32)	1.837	0.185	0.054
WRECALL				
Time	(3, 96)	5.948	0.001**	0.157
Time*Group	(3, 96)	1.387	0.252	0.042
Group	(1, 32)	0.761	0.389	0.023
WRECOG				
Time	(3, 87)	3.547	0.018 *	0.109
Time*Group	(3, 87)	1.226	0.305	0.041
Group	(1, 29)	1.898	0.061	0.061
STROOP1				
Time	(2.061, 61.821)	0.627	0.542	0.020
Time*Group	(2.061, 61.821)	0.268	0.773	0.009
Group	(1, 30)	9.075	0.005 **	0.232
STROOP INT				
Time	(1.901, 66.521)	2.28	0.113	0.061
Time*Group	(1.901, 66.521)	1.68	0.195	0.046
Group	(1, 35)	7.004	0.012 *	0.167
WCSTNCORR				
Time	(2.452, 83.379)	1.351	0.265	0.038
Time*Group	(2.452, 83.379)	1.460	0.236	0.041
Group	(1, 34)	9.101	0.005 **	0.211
WCSTCAT				
Time	(3, 102)	2.231	0.089	0.062
Time*Group	(3, 102)	1.567	0.202	0.044
Group	(1, 34)	11.457	0.002 **	0.252
SDSTNCORR				
Time	(2.122, 67.900)	7.715	0.001 **	0.194
Time*Group	(2.122, 67.900)	1.117	0.336	0.034
Group	(1, 32)	14.109	0.001 **	0.306
SDSTIT				
Time	(1.449, 46.354)	0.337	0.646	0.010
Time*Group	(1.449, 46.354)	2.287	0.127	0.067
Group	(1, 32)	0.536	0.469	0.016
SDSTMT				
Time	(2.127, 68.064)	4.956	0.009 **	0.134
Time*Group	(2.127, 68.064)	6.832	0.446	0.025
Group	(1, 32)	5.440	0.026 *	0.145
CLIT				
Time	(3, 93)	1.901	0.135	0.058
Time*Group	(3, 93)	1.642	0.185	0.050
Group	(1, 31)	10.761	0.003 **	0.258
CLMT				
Time	(1.273, 42.002)	6.479	0.010 *	0.164
Time*Group	(1.273, 42.002)	0.927	0.364	0.027
Group	(1, 33)	7.674	< 0.001 **	0.189
CCIT				
Time	(2.350, 17.035)	2.011	0.133	0.057
Time*Group	(2.350, 17.035)	0.513	0.630	0.015
Group	(1, 33)	6.140	0.019 *	0.157
CCMT				
Time	(2.494, 82.315)	3.989	0.015 *	0.108
Time*Group	(2.494, 82.315)	0.255	0.822	0.008
Group	(1, 33)	6.369	0.017 *	0.162

* $p = 0.05$;
** $p = 0.01$.

and psychomotor functioning. Although this could not be statistically established because of the limited sample, explorative analyses indicated that patients with high scores on SDST did not differ from controls on cognitive and psychomotor measures, though exhibiting the same level of depression as the low score group. The subtype of so-called late life depression and/or the subtype with a dysexecutive syndrome, are known to show more lasting psychomotor and cognitive, especially executive, symptoms. Executive dysfunction happens to be the symptom that predicts bad prognosis in treatment with escitalopram. In our baseline study (Beheydt et al., 2015), it became clear that executive dysfunction is typical for depression, and slow processing speed for aging. In our present study, we found that following treatment with escitalopram, some executive functions (Stroop INT) improve, but only in the low level processing speed group. As in comparison to the control group, high level processing speed patients were hardly impaired from the start, a ceiling effect prevented improvement (Fig. 1). The additive effect of aging and depression on cognitive and psychomotor retardation seems to be an aging – perhaps comorbidity – effect of disturbed processing speed.

Finally, even if an important limitation of the study is the large number of excluded patients and drop outs, studying depressed elderly remains necessary, given the observed specific functional impairing effect of depression in such a population. Rigidly eliminating possible effects of other psychotropic medication, showed, moreover, that elderly depression entails long lasting motor impairment going along with specific cognitive defects, particularly in processing speed and executive function. Marked differences in response between core symptoms seems to be peculiarly age related, as, in younger patients with severe psychomotor retardation, mood symptoms generally improve right after psychomotor symptoms and not long before. The interaction effect of physical health, aging and depression, therefore, demands increased attention. However, in geriatric depression, permanent mild cognitive impairment and psychomotor retardation as a result of comorbidity should always be taken into account. The differentiated assessment of core symptoms to evaluate effectivity of antidepressants in elderly patients clearly appears necessary.

Role of funding source

None of the funders had any role in study design, data collection, data analysis, manuscript preparation or submission of this manuscript.

Conflict of interest

This study was supported originally by a grant of Lundbeck.

Acknowledgments

This research was supported by a special fellowship of the FWO research fund Flanders (Number 1901315N). The authors are grateful to all participants for their time and effort and to the University Psychiatric Centers of the Psychiatric Center of Duffel and the University Psychiatric Center KULeuven. We would also like to thank Marieke Impens, Sara Vermeylen and Dr. Jules Janssens involved in the data acquisition.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jad.2015.08.041.

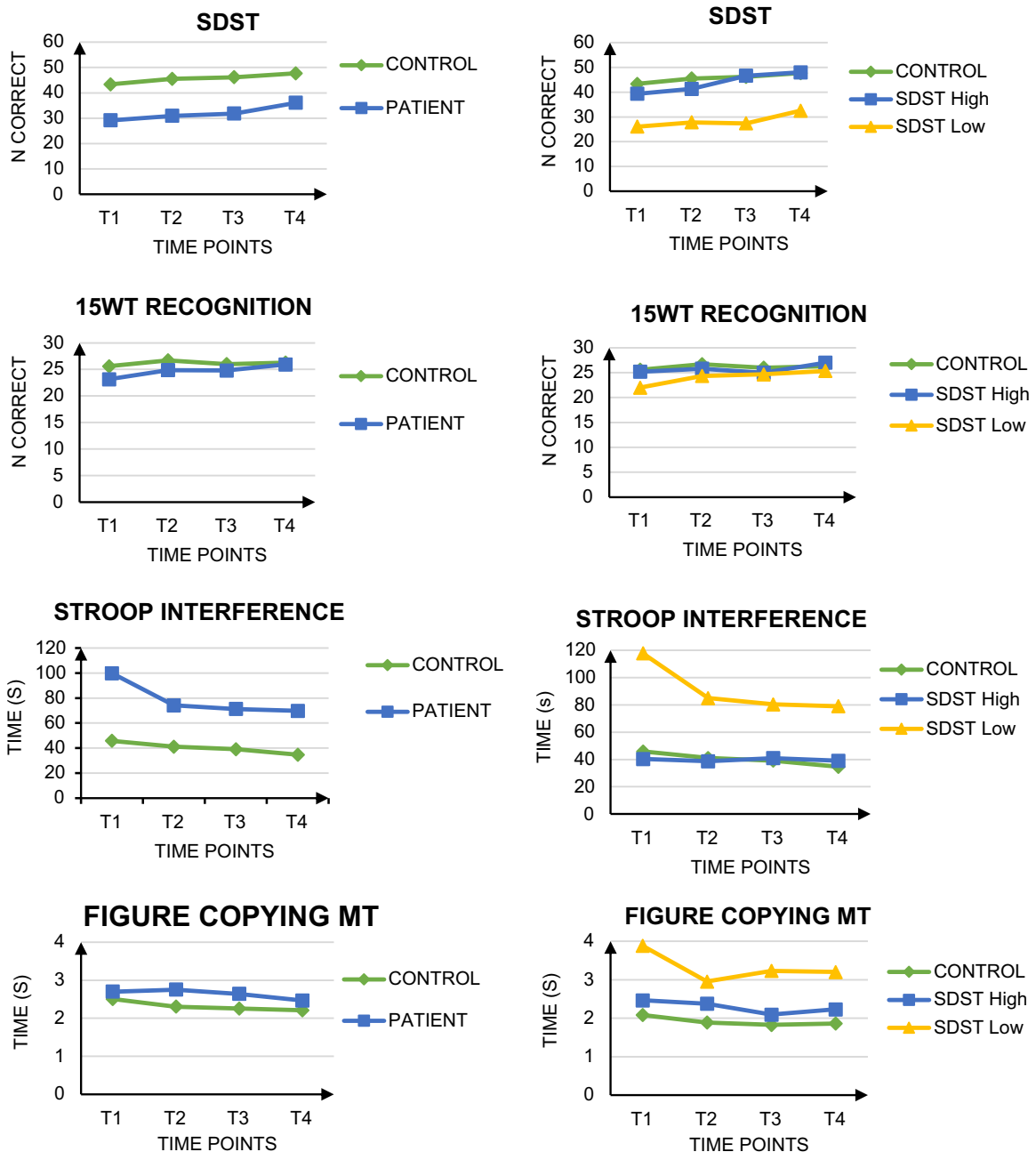

Fig. 1. Limited interaction effects were found but also subgroups of high and low score (separated by the median) on SDST in patients.

References

Alexopoulos, G.S., Borson, S., Cuthbert, B.N., Devanand, D.P., Mulsant, B.H., Olin, J.T., Oslin, D.W., 2002. Assessment of late life depression. Biol. Psychiatry 52 (3), 164–174.

Barceló, F., Knight, R.T., 2002. Both random and perseverative errors underlie WCST deficits in prefrontal patients. Neuropsychologia 40 (3), 349–356.

Beheydt, L.L., Schrijvers, D., Docx, L., Bouckaert, F., Hulstijn, W., Sabbe, B., 2015. Psychomotor retardation in elderly untreated depressed patients. Front. Psychiatry 5 (196). http://dx.doi.org/10.3389/fpsyt.2014.00196.

Bennabi, D., Vandel, P., Papaxanthis, C., Pozzo, T., Haffen, E., 2013. Psychomotor retardation in depression: a systematic review of diagnostic, pathophysiologic, and therapeutic implications. Biomed. Res. Int. 2013, 158746.

Bose, A., Li, D., Gandhi, C., 2008. Escitalopram in the acute treatment of depressed patients aged 60 years or older. Am. J. Geriatr. Psychiatry 16 (1), 14–20.

Buyukdura, J.S., McClintock, S.M., Croarkin, P.E., 2011. Psychomotor retardation in depression: biological underpinnings, measurement, and treatment. Prog. Neuropsychopharmacol. Biol. Psychiatry 30 (2), 395–409. http://dx.doi.org/10.1016/j.pnpbp.2010.10.019 35.

Chen, T.Y., Peronto, C.L., Edwards, J.D., 2012. Cognitive function as a prospective predictor of falls. J. Gerontol. Ser. B: Psychol. Sci. Soc. Sci. 67 (6), 720–728. http://dx.doi.org/10.1093/geronb/gbs052.

Cipriani, A., Furukawa, T.A., Salanti, G., Watanabe, N., Nakagawa, A., Omori, I.M., Mc Guire, H., Tansella, M., Barbui, C., 2009. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. Lancet 373, 746–758.

Culang, M., Sneed, J.R., Keilp, J.G., Rutherford, B.R., Pelton, G.H., Devanand, D.P., Roose, S.P., 2009. Change in cognitive functioning following acute antidepressant treatment in late-life depression. Am. J. Geriatr. Psychiatry 17 (10), 881–888.

Field, A., 2009. Discovering Statistics Using SPSS, Third edition. Sage Publications, London.

Gorwood, P., Weiler, E., Lemming, O., Katona, C., 2007. Escitalopram prevents relapse in older patients with major depressive disorder. Am. J. Geriatr. Psychiatry 15 (7), 581–593.

Greden, J.F., Carroll, B.J., 1981. Psychomotor function in affective disorders: an overview of new monitoring techniques. Am. J Psychiatry 138 (11), 1441–1448.

Greve, K.W., Bianchini, K.J., Mathias, C.W., Houston, R.J., Crouch, J.A., 2002. Detecting malingered performance with the Wisconsin card sorting test: a preliminary investigation in traumatic brain injury. Clin. Neuropsychol. 16 (2), 179–191.

Hamilton, M., 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62.

Hegerl, U., Mergl, R., Henkel, V., Pogarell, O., Muller-Siecheneder, F., Frodl, T., Juckel, G., 2005. Differential effects of reboxetine and citalopram on hand-motor function in patients suffering from major depression. Psychopharmacology (Berl) 178, 58–66.
Kalayam, B., Alexopoulos, G., 1999. Prefrontal dysfunction and treatment response in geriatric depression. Arch. Gen. Psychiatry 56, 713–718.
Kasper, S., De Swart, H., Frijs Andersen, H., 2005. Escitalopram in the treatment of depressed elderly patients. Am. J. Geriatr. Psychiatry 13, 884–891.
Kok, R., Verhey, F., 2002. Gestandaardiseerde Mini-Mental State Examination. Dutch translation of the Mini Mental State Examination. (Folstein et al., 1975), Janssen, Belgium.
Kok, R.M., Nolen, W.A., Heeren, T.J., 2012. Efficacy of treatment in older depressed patients: a systematic review and meta-analysis of double-blind randomized controlled trials with antidepressants. J. Affect. Disord. 141, 103–115.
Lockwood, K.A., Alexopoulos, G.S., van Gorp, W.G., 2002. Executive function in geriatric depression. Am. J. Psychiatry 159, 1119–1126.
Maarse, F.J., Janssen, H.J., Dexel, F., 1988. A special pen for an XY-tablet. In: Maarse, F.J., Mulder, L.J.M., Sjouw, W.P.B., Akkerman, A.E. (Eds.), Computers in Psychology: Methods, Instrumentation and Psychodiagnostics. Swets Zeitlinger, Amsterdam, pp. 133–139.
Mao, P.X., Tang, Y.L., Jiang, F., Shu, L., Gu, X., Li, M., Qian, M., Ma, C., Mitchell, P.B., Cai, Z.J., 2008. Escitalopram in major depressive disorder: a multicenter, randomized, double-blind, fixed-dose, parallel trial in a Chinese population. Depression Anxiety 25 (1), 46–54.
Mc Leod, C.M., 1991. Half a century of research on the Stroop effect: an integrative review. Psychol. Bull. 109, 163–202.
Mc Leod, D.R., Griffiths, R.R., Bigelow, G.E., Yingling, J., 1982. An automated version of the digit symbol substitution test (DSST). Behav. Res. Methods Instrum. Comput. 14, 463–466.
Mergl, R., Juckl, G., Rihl, J., Henkel, V., Karner, M., Tigges, P., Schroter, A., Hegerl, U., 2004. Kinematical analysis of handwriting movements in depressed patients. Acta Psychiatr. Scand. 109, 383–391.
Mitchell, A.J., Subramaniam, H., 2005. Prognosis of depression in old age compared to middle age: a systematic review of comparative studies. Am. J. Psychiatry 162 (9), 1588–1601.
Parker, G., Roy, K., Hadzi-Pavlovic, D., Wilhelm, K., Mitchell, P., 2000. The differential impact of age on the phenomenology of melancholia. Psychological Medicine 31 (7), 1231–1236.
Parker, G., Roy, K., Mitchell, P., Wilhelm, K., Menkes, D.B., Snowdon, J., Schweitzer, I., Grounds, D., Skerritt, P., Roy, K., Hadzi-Pavlovic, D., 2000. Sub-typing depression by clinical features: the Australian database. Acta Psychiatr. Scand. 101, 21–28.
Roose, S.P., Sackeim, H.A., Krishnan, K.R.R., Pollock, B.G., Alexopoulos, G., Lavretsky, H., Katz, I.R., Hakkarainen, H., 2004. Antidepressant pharmacotherapy in the treatment of depression in the very old: a randomized, placebo-controlled trial. Am. J. Psychiatry 161, 2050–2059.
Saan, R.J., Deelman, B.G., 1986. De 15-woordentest A en B, een voorlopige handleiding. Groningen: Afdeling Neuropsychologie, AZG.
Sabbe, B., van Hoof, J., Hulstijn, W., Zitman, F., 1996. Changes in fine motor retardation in depressed patients treated with fluoxetine. J. Affect. Disord. 40, 149–157.
Santos, K.T., Fernandes, M.H., Reis, L.A., Coqueiro, R.S., Rocha, S.V., 2012. Depressive symptoms and motor performance in the elderly: a population based study. Rev. Bras. Fysioterapia 16, 295–300.
Schrijvers, D., Hulstijn, W., Sabbe, B.G.C., 2008. Psychomotor symptoms in depression: a diagnostic, pathophysiological and therapeutic tool. J. Affect. Disord. 109, 1–20.
Schrijvers, D., Maas, Y., Pier, M.P.B.I., Madani, Y., Hulstijn, B.C.G., Sabbe, B.G.C., 2009. Psychomotor changes in major depressive disorder during sertraline treatment. Neuropsychobiology 59, 34–42.
Sneed, J.R., Culang, M.E., Keilp, J.G., Rutherford, B.R., Devanand, M.D., Roose, S.P., 2010. Antidepressant medication and executive dysfunction: a deleterious interaction in late-life depression. Am. J. Geriatr. Psychiatry 18 (2), 128.
Sobin, C., Sackeim, H.A., 1997. Psychomotor symptoms of depression. Am. J. Psychiatry 154, 4–17.
Spielberger, C.D., Gorsuch, R.L., Lushene, R., Vagg, P.R., Jacobs, G.A., 1983. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA, Consulting Psychologists Press. Palo Alto.
Topiwala, A., Chouliaras, L., Ebmeier, K.P., 2014. Prescribing selective serotonin reuptake inhibitors in older age. Maturitas 77, 118–123.
Widlöcher, D., Ghozlan, A., 1989. The measurement of retardation in depression. In: Hindmarch, I., Stonier, P.D. (Eds.), Human Psychopharmacology: Measures and Methods vol. 2. Wiley, New York.
Yesavage, J.A., Brink, T., 1982. Development and validation of a geriatric depression screening scale. A preliminary report. J. Psychiatr. Res. 17, 37–49.

Lieve Beheydt – was involved in every stage of study from the design of the study, the experimental testing, data analysis and interpretation and writing the manuscript.

Didier Schrijvers – contributed to the design of the study, and interpretation of the data. He also revised the manuscript critically.

Lise Docx – contributed to the design and conduct of the experiments as well as to the critical revision of the manuscript.

Filip Bouckaert – made a substantial contribution to recruit patients and to make clinical assessments and diagnoses; he also revised the manuscript critically.

Wouter Hulstijn – made a substantial contribution to the analysis of the data and the interpretation of the data. In addition, he was very involved in revision of the paper.

Bernard Sabbe- substantially contributed to the conception of the study and its design. In addition, he was involved in critically revising the manuscript.