



*The influence of methylphenidate on the
severity of stuttering: a randomized controlled
trial*

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Master in de Geneeskunde

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ABSTRACT

BACKGROUND: Recently a case report described a non-expected decrease in severity of stuttering after intake of methylphenidate (MPH). This study was undertaken to investigate if this effect also could again be reproduced in a population of healthy male participants with developmental stuttering (PWDS).

METHODS: A double-blind randomized cross-over trial with a two week wash-out period including 15 Dutch speaking young healthy PWDS assessed the effects of a single doses of 20mg MPH compared to placebo on their stuttering. A dependent and a one sample t-test have been used to detect significant differences. The endpoint was the number of stutter moments and the self-perceived improvement.

RESULTS: MPH gave a significant improvement of the number of stutter moments when reading and speaking ($P= 0,002$), which was not the case with placebo ($P= 0,090$). There was a significant improvement from baseline after intake of MPH compared to placebo ($P=0,003$). The self-perceived improvement with MPH was not significant better compared to placebo ($P= 0,28$).

CONCLUSION: This study showed that the participants had an objective statistically significant improvement of the severity of stuttering with MPH and this was not the case with placebo. This was the case for a reduction in stutter moments and for an improvement when reading out loud and speaking spontaneously. However, this result was not subjectively perceived by the participants, probably because they had high expectations of the study and would only perceive a complete remission of stuttering as a subjective improvement.

KEYWORDS: developmental stuttering; methylphenidate; stuttering

INTRODUCTION

Prevalence and incidence

Developmental stuttering (DS) is a disorder of speech fluency. It has a gradual onset around the age of two to seven years when the children are still learning speech and language skills. DS consists of blockage of the vocal tract, repetitions of sounds, syllables and monosyllabic words as well as sound prolongations. (1, 2)

Other types of stuttering, that are not DS, are neurogenic (concomitant to a brain lesion) and psychogenic (when the stuttering is a direct consequence of a psychological trauma).

Stuttering is a worldwide problem that affects about 5% of all children, especially males. (3, 4) The actually most current hypothesis about this difference in gender prevalence is that the myelinisation around the nerves develops in a later stage with boys. (5)

Most of the children who stutter will recover by speech therapy or spontaneously during childhood, leaving about 1% of the population with persistent developmental stuttering (PDS). (2, 4)

There exists a lot of different theories of stuttering (disturbance of rhythm, respiratory muscles, coordination, auditory feedback, fluent speech, motor timing, cerebral dominance, abnormal activation of auditory cortex and the left hemisphere speech area with implication of the cerebellum, deficiencies of left grey matter and reduced white matter and atypical functioning of the planum temporale in relation to altered auditory feedback). (6)

Quality of life

Moderate to severe stuttering affects the quality of life negatively and the adults who stutter (AWS) following therapy rate their stuttering as more severe. (7)

AWS experience blockages, tension and repetitions of sounds, syllables and words as important factors for the severity of stuttering as well as the emotions which the AWS experiences during stuttering.

Causes

Stuttering can be seen as a multifactorial disease. The exact pathophysiology of developmental stuttering is still unknown because the influence of both nature and nurture can be observed.

Although DS may be worse by stressful situations, there is no evidence that anxiety or conflicts cause DS. (8)

The emotions in these stressful situations probably provoke a temporary imbalance in the basal ganglia by a dysfunction of the dopamine release from the substantia nigra to the striatum. This provokes temporary stuttering and other involuntary movements by a loss of inhibitory control.

Each situation in which stuttering is experienced would reinforce this circuit and give rise to stutter reaction and so on, which is called the feed forward loop. (6)

Genetic causes

In most of the AWS there is no genetic cause found or is not yet fully understood. Gene mutations that appear to be relevant to DS are N-acetylglucosamine-1-phosphate transferase, alpha and beta subunits (GNPTAB), N-acetylglucosamine-1-phosphate transferase, gamma subunit (GNPTG) and N-acetylglucosamine-1-phosphodiester alpha-N-acetylglucosaminidase (NAGPA) which are responsible for about 9% of cases of stuttering. (6, 9)

GNPTG gene is mainly associated with European and Asian populations, whereas GNPTAB is associated with Pakistani families. Several autosomal chromosomes such as 1,3,5,9,12,13,15,18 are related to DS, whereas 5 and 15 have been identified in connection with PDS. (10)

Another genetic cause in stuttering appears to be polygenic due to dopamine 2 (D2) receptor, dopamine beta hydroxylase and the dopamine transporter. (11)

Speech therapy

Speech therapy is the main treatment option for the moment, but a lot of the severe cases of DS and those who were treated after puberty will recover only partially or will be refractory. (12)

The different viewpoints in the treatment of PDS are building self-esteem, avoidance reduction and making an attitude change or systematic application of the steps and rules of speech mechanisms and attempts to reconstruct the respiratory, phonatory and articulatory gestures used to generate speech. (13)

Methylphenidate (MPH)

In 1962 Fish et al. concluded that D-amphetamine had a beneficial effect on stuttering but it was never implemented in clinical practice because of severe adverse events. (14) Fifty year later a case report described the decrease in severity of stuttering after intake of a single dose of 20mg methylphenidate, an amphetamine analogue with less severe side effects, in a young healthy male. (15)

Aim of the study

This study investigated the hypothesis that the administration of MPH in a population of healthy male participants with developmental stuttering reduces the severity of stuttering compared to the administration of placebo.

METHODS

Clinical Design

The study design was an double-blind, placebo-controlled crossover randomized trial (RCT) with MPH. All subjects were Belgian Dutch speaking AWS, who continued to stutter after speech therapy. Participants were recruited through national media (press releases and radio). The clinical trial was conducted at the Free University of Brussels between February and March 2014.

Figure 1 is a flow diagram of enrollment and participation of AWS. From 489 subjects that showed interest in participating in the study, 473 were excluded: 377 did not meet the inclusion/exclusion criteria and 96 were not available on the date of the study. Sixteen subjects agreed to participate in the study, of which 1 participant dropped out because he was not available on the second day of the

trial. Full data of 15 subjects were obtained. Table 1 shows the disfluency frequencies of those 15 analyzed subjects.

Inclusion and Exclusion Criteria

Eligible participants were men aged 18 to 40 years with developmental stuttering. Participants were excluded if they met any of the following criteria: psychogenic or neurogenic stuttering, antecedents or known psychological disorders, ADHD, narcolepsy, pregnancy, glaucoma, hyperthyroid, epilepsy, alcoholism, stroke or TIA, cocaine usage, medication abuse, liver disease, hypertension and daily usage of any sort of medication.

Intervention

Participants were divided at random in two groups, whereby the first group received 20mg (2 tablets of 10mg) MPH and the other group two tablets placebo. Participants were instructed to take both tablets orally. After a wash-out period of two weeks, the group which received the active medicine MPH received the placebo and vice versa. All the tablets were pre-packed into a white package which looked the same for both medications.

Outcome Measures

The participants were asked to read out loud a Dutch standardized text of 331 words (Text 1) (16) and speak for about five minutes spontaneously. This examination was performed each time before and two hours (peak action of MPH) after intake of the medication.

After intake of the medication, the participants were asked if they thought they had received MPH or placebo to control the blinding of this study. The participants were also asked how they perceived their speech (worse, the same or better), to compare it between intake of MPH or placebo.

All the examinations were video-taped and used to count the number of stuttering moments (repetitions, blocks and sound elongations) to assess the severity of the stuttering. The total amount of stuttering moments during the examination and for the component reading and spontaneous

speech apart, after intake of the pills, were compared with the baseline that was obtained from the examination before intake of the pills. Only one minute around the middle of the five minutes spontaneous speech with every participant was counted to avoid more stuttering moments when starting to speak and when the participant became more tired or began to use well-known expressions to fill up the time.

Recording the frequency, duration and physical tension of stuttered words in conversational speech and in oral reading task in a group of Dutch speaking people who stutter and non-stutter has a sensitivity of 93,45% and a specificity of 100%. (17)

Randomization

Each participant was assigned to a number on a list conformable the appointment with the investigator. Each number on the list was randomly assigned to one or the other group of the medication the participant received that day. The randomization key was kept off-site. The investigator could only request the randomization code of a participant in the event of medical emergency, which did not occur. The randomization key was provided after the completion of the trial and after counting all the participants stuttering moments.

Study approval

This study was approved by the ethical committee of the Free University of Brussels (2013/284), the Federal Agency for Medication and Medical products (FAGG). An informed consent (Text 2) was obtained from each participant. This study was registered with EudraCT (2013-004206-26).

Statistical Analysis

A dependent t-test (paired-samples t-test) was used to compare the means between the two related groups on a same continuous, dependent variable. A one-sample t-test was used on the percent improvement correction for baseline differences. The percent improvement was calculated by the difference in number of stutter moments before and after intake of medication or placebo, divided

by the number of stutter moments before intake. A P-value < 0.05 was considered statistically significant.

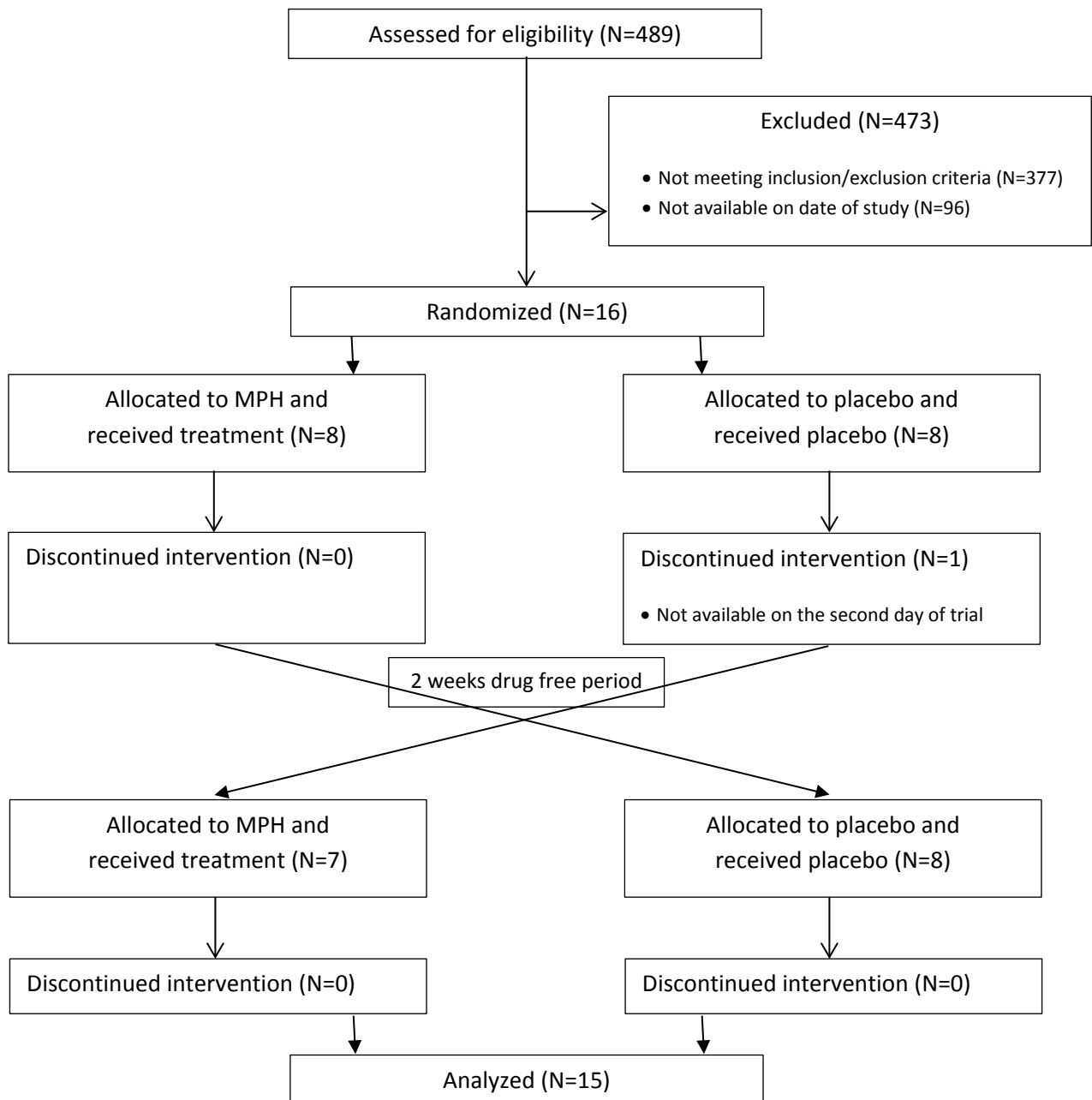


Figure 1 - Flow diagram of enrollment and participation of AWS
MPH: methylphenidate, N= number

RESULTS

All 15 participants were Belgian Dutch speaking AWS, who already underwent speech therapy. The age of the participants was between 19 and 35 years old, with a mean age of 28 and a median of 27 years old.

Reading

The participants who had received MPH had an average of 33 stutter moments before intake and an improvement of 11 stutter moments (standard deviation (SD) = 12) after intake of MPH. The improvement for MPH was statistically significant ($P= 0.003$). Those who had received placebo had an average of 30 stutter moments at baseline and an improvement of 4 (SD= 8). The improvement after intake of placebo was not significant ($P= 0.061$). There was no significant difference in baseline before MPH and placebo ($P= 0.26$).

Speaking

For speaking there was a more variable baseline where the participants had an average of 13 stutter moments before placebo and an average of 19 stutter moments before intake of MPH. MPH gave an average improvement of 11 stutter moments whereas placebo did not give an improvement but instead an average deterioration of two stutter moments. The improvement after MPH was statistically significant ($P= 0.020$). The deterioration after placebo was not significant ($P= 0.17$).

Composed endpoint of reading and speaking

The baseline before placebo (42 stutter moments) and before MPH (53 stutter moments) were not statistically significant ($P= 0.090$). Placebo had an average improvement of three stutter moments ($P= 0.29$) which was not statistically significant. Intake of MPH had an average improvement of 22 stutter moments which was statistically significant with the baseline ($P= 0.002$).

Treatment assumption

Eight of 15 participants thought having taken the wrong medication when asked what they had

received. Three of them thought they had received placebo and five of them thought they had received MPH when in reality they had received the opposite. Only seven of the 15 participants did guess correctly.

We did not find a significant influence for reading and speaking based on what the participant thought he had received. (Table 4 in appendices)

Learning effect

Between the first session before medication intake and the second session before medication intake the participants showed a not significant improvement of five stutter moments during reading (from 34 to 29) with a p-value of 0.13. When speaking they also did not show a not significant improvement with only two stutter moments (from 17 to 15) and a p-value of 0.50. Table 2 shows we could not demonstrate a significant adaptation effect in the second session when the participant had read the text for the third time.

Self-perceived improvement

Nine of 15 participants found that MPH gave a subjective improvement but nine of 15 participants also found that placebo gave a subjective improvement of their stuttering. MPH did not give a statistically difference in subjective improvement comparison with placebo ($P = 0,28$).

Percent improvement

Because of the significant difference in baseline measurement for speaking between MPH and placebo, we also conducted an analysis with the relative percent improvement of stutter moments (Table 3).

This showed an average improvement when reading of 44% after MPH intake and a deterioration of 4,7% after placebo intake. The improvement with MPH was statistically significant compared to those with placebo ($P = 0,028$). For speaking, the participants had an improvement of 54% when using MPH and a deterioration with placebo of 56%, which translates in a strong statistically significant better result with MPH compared to placebo ($P < 0,001$).

When using placebo the participants had a deterioration of 14% and an improvement of 46% when using MPH for reading and speaking. The percent improvement of stuttering when reading and speaking with MPH was statistically significant better than with placebo (P= 0,003).

Table 1 – Descriptives and outcomes on absolute number of stutter moments

		Placebo	MPH	p-value
Reading				
Baseline	mean±SD	30±37	33±44	0,26
After intake	mean±SD	25±30	23±39	
Difference	mean±SD	4±8	11±12	
Difference	p-value	0,061	0,003	
Speaking				
Baseline	mean±SD	13±15	19±24	0,042
After intake	mean±SD	14±12	8±9	
Difference	mean±SD	-2±4	11±17	
Difference	p-value	0,17	0,020	
Reading and speaking				
Baseline	mean±SD	42±42	53±60	0,090
After intake	mean±SD	40±35,21	31±42	
Difference	mean±SD	3±9	22±22	
Difference	p-value	0,29	0,002	

SD= Standard deviation, MPH= Methylphenidate
p-value and SD were calculated on the unrounded values of the dataset. The averages and SD were rounded.

Table 2 – Descriptives and outcomes of the 2 sessions

		Session 1	Session 2	p-value
Reading				
Baseline	mean±SD	34±45	29±36	0,13
Speaking				
Baseline	mean±SD	17±25	15±14	0,50
Reading and speaking				
Baseline	mean±SD	51±61	44±42	0,24

SD= Standard deviation

p-value and SD were calculated on the unrounded values of the dataset. The averages and SD were rounded.

Table 3 – Descriptives and outcomes of percent improvement corrected for baseline differences

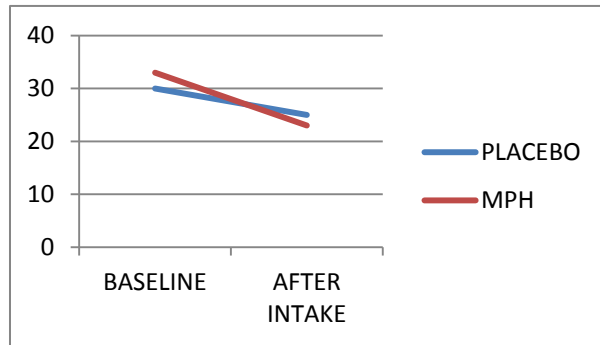
		Placebo	MPH	p-value
Reading				
% improvement	mean±SD	-0,047±0,6	0,44±0,3	0,028
	p-value	0,76	<0,001	
Speaking				
% improvement	mean±SD	-0,56±0,8	0,54±0,3	<0,001
	p-value	0,017	<0,001	
Reading and speaking				
% improvement	mean±SD	-0,14±0,6	0,46±0,2	0,003
	p-value	0,34	<0,001	

SD= Standard deviation, MPH= Methylphenidate

p-value and SD were calculated on the unrounded values of the dataset. The averages and SD were rounded.

Line chart 1 -

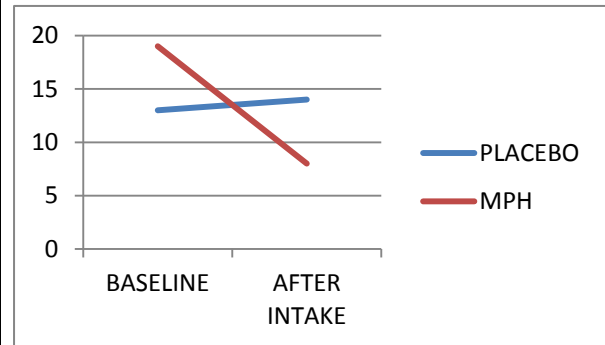
Number of stutter moments when reading



MPH= Methylphenidate

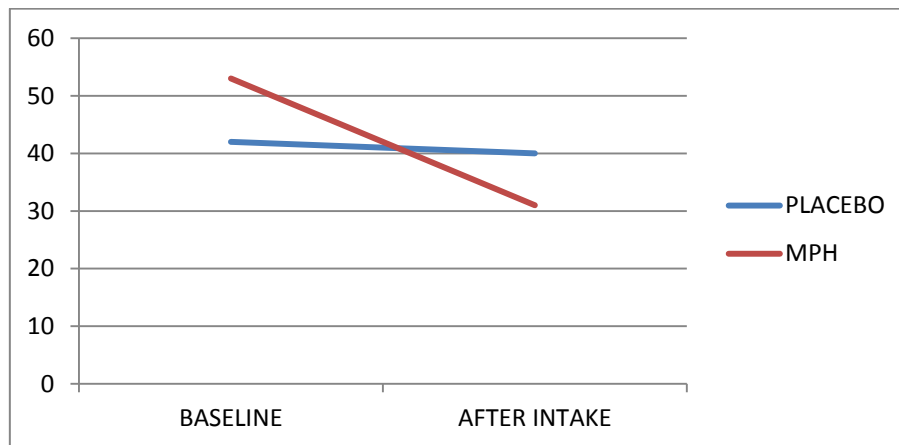
Line chart 2 -

Number of stutter moments when speaking



MPH= Methylphenidate

Line chart 3 - Number of stutter moments when reading and speaking



MPH= Methylphenidate

DISCUSSION

This study showed that the participants had an objectively statistically significant improvement of the severity of stuttering with a single dose MPH and this was not the case with placebo. This was the case with an absolute reduction in stutter moments and with a percentage improvement when reading out loud and speaking spontaneously.

However, this result was not subjectively perceived in that way, which could probably be due to the fact

that the participants would only perceive their stuttering as improved when it is in complete remission and not when they stutter less than before.

Comparison with other studies

An double blind study in 1962 noticed a considerable reduction of stutter moments after intake of D-amphetamine for a three-month period with mentally retarded AWS. (14)

A systemic review reviewed articles from 1970 to 2005 concerning medical treatment for stuttering with carbamazepine, phenelzine, paroxetine, sertraline, mianserin, clomipramine, haloperidol, olanzapine, risperidone, clonidine, oxprenolol, propranolol, verapamil, bethanechol, pimoziide, tiapride, botulinum toxin and alprazolam with citalopram. The recommendations were uniformly negative for all the pharmacological agents due to side effects, other risks and poor effectiveness. The review did not conclude that none of the participants received any benefit, but that none of the tested pharmacological agents for stuttering could be recommended for general use. (18)

There has been some studies that showed that a hyperdopaminergic situation in the brain provokes stuttering. (8) The role of dopamine 1 (D1) and D2 receptors is still unknown. Some AWS go better with D1 blockers or D2 blockers and others worsen. (11) MPH appear to have an indirect stimulation of D1 receptors in the prefrontal cortex (19) and a decrease in D2 receptors. (20, 21)

Although MPH is often viewed as a safe drug with little addiction potential, emerging evidence indicates that MPH abuse is common and increasing. (22, 23)

Strengths and limitations

The results of this study need to be interpreted in consideration of some methodological limitations.

This study used a small sample size of 15 participants. Participants were healthy, between 19 and 35 year old and from the male sex. These results may not be generalizable to people with other characteristics.

This study only included male subjects. The effect of hormones on stuttering is not yet fully investigated and therefore it is not sure that the results of this study can be extrapolated to the female population.

In general, MPH improved stuttering clearly in some of the participants. But in some patient MPH seemed to have little or no effect, but we do not know why. It might be that this difference in reaction is due to a difference in stuttering sub group, because we know that the group of developmental stutters is a heterogeneous group with different pathways that give rise to the stuttering speech. More investigation in the subgroups and different pathways in developmental AWS is necessary.

All the video recordings were counted by the same observer, but there has been no audit from another observer to obtain an intra-observational comparison.

Each time the same text was used to read out loud and there could be a learning effect which could have given rise to less stutter moments after reading the text for multiple times. There was no significant difference found in the amount of stutter moments between the baseline before the first and the second session. This could be attributed to the fact that the reading text has no predictable progress. Most participants told us that the text made little sense to them.

We did not find a significant difference at baseline for reading, but we did find a significant different number of stutter moments for spontaneous speech before intake of MPH and placebo. To solve this baseline difference, we also used in our analyses a percentage improvement after medication intake which gave the same conclusion as with the absolute improvement of stutter moments.

An improvement in cognitive performance concerning working and speed of processing is seen in a healthy population after receiving a single dose of MPH. To a lesser extent there can also be found an improvement of verbal learning, attention, vigilance, reasoning and problem solving. (24)

We used a single dose MPH, the effects of daily intake on stuttering are not investigated in this study. But it is not certain that a daily dose is necessary for all the AWS. It could be possible that the breaking of the forward loop could be sufficient therapy.

The amount of stutter moments changes during and between days which makes it hard to know for sure that the seen improvement in this study is caused by MPH and not by a fluctuation.

Future

Further long-term investigation is necessary to know what the effects of daily intake of MPH would be on stuttering and which subgroups and different pathways exist for developmental stuttering. We also advise to investigate if MPH would have a positive effect on the severity of stuttering of female AWS. It would also be interesting to determine a safety profile of MPH for long-time use, taking into account the possible addictive effect during treatment.

CONCLUSION

This randomized controlled trial with 15 participants showed a significant decrease of the number of stutter moments after intake of MPH and no significant improvement after the intake of placebo.

This study could not demonstrate a self-perceived significant improvement of stuttering either after MPH or placebo intake.

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Also I would like to thank the participants in this study, who gave up their time to investigate the

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APPENDICES

Tabel 4 – Descriptives and outcomes based on what the participant thought he had received

Thought he had received		Placebo	MPH	p-value
Reading				
Baseline	mean±SD	32±45	31±36	0,78
After intake	mean±SD	24±39	24±31	
Difference	mean±SD	8±12	7±9	
Difference	p-value	0,020	0,010	
Speaking				
Baseline	mean±SD	18±24	14±15	0,14
After intake	mean±SD	11±8	12±13	
Difference	mean±SD	8±19	2±4	
Difference	p-value	0,13	0,095	
Reading and speaking				
Baseline	mean±SD	50±61	45±42	0,36
After intake	mean±SD	34±41	36±37	
Difference	mean±SD	16±26	9±10	
Difference	p-value	0,031	0,004	

SD= Standard Deviation

p-value and SD were calculated on the unrounded values of the dataset. The averages and SD were rounded.

Text 1 - De Kapitein (Nederlands)(16)

De kapitein zit op het terras van het café “Het witte paard”, achter een pint schuimend bier. Recht voor hem, aan de overzijde van de weg, buigt rijpend koren naar de grond. Het is een warme, broeierige dag. In de namiddag zijn in de verte donderkoppen komen opzetten.

Het onweer is losgebarsten, plots en hevig, maar na regen komt zonneschijn. Nu zijn de wolken weer verdwenen en is de lucht opnieuw blauw. Een blauw dat langzaam, bijna onmerkbaar donkerder wordt.

De zon hangt laag over de bossen in de verte. Het rode licht weerkaatst in de rivier. Samen met de zon glijdt de dag naar de avond toe. Straks ontmoeten dag en avond elkaar en wordt het weer nacht. Eén van die zomernachten waarin men moeilijk de slaap vindt.

De kapitein heeft zijn koppelriem losgemaakt en die ligt nu op de tafel naast zijn glas bier. De waard, die hem daarnet zijn glas bezorgde, is terug binnengegaan. De kapitein houdt niet van veel gepraat. Het harde leven dat hij achter de rug heeft, maakte van hem een zwijger. Een denker, die genoeg heeft aan eigen gedachten.

Het is nu reeds twee weken geleden dat de kapitein en zijn manschappen hier aangekomen zijn. De overname van het dorp gebeurde met veel pracht en praal. Er werden redevoeringen gehouden over internationale samenwerking ten voordele van gans de mensheid. Pers en televisie waren aanwezig. Daarna is alles weer rustig geworden in het dorp. Even rustig als voorheen. Een rust die lijkt op een stilte voor de storm.

Voor de kapitein zijn het tot nu toe drukke, volzette dagen geweest. Hij heeft eerst voor zijn eigen inkwartiering moeten zorgen en ook voor die van zijn manschappen. Uit de leegstaande huizen heeft hij een goede keuze kunnen doen. Zijn mannen zijn deftig gelogeerd in twee aan elkaar palende woningen, op het plein voor de kerk. Voor zichzelf heeft hij een afzonderlijke woning in één van die huizen. Zodoende leeft, eet en slaapt hij met zijn manschappen.

Text 2 - Toestemming tot deelname aan wetenschappelijk onderzoek (Informed consent)

Beste deelnemer,

Op dit moment wordt stotteren behandeld met stottertherapie bij een logopedist(e). In de literatuur is echter een hypothese gemaakt over ontwikkelingsstotteren waarbij een stof in de hersenen (dopamine genaamd) een cruciale rol zou spelen in de spraak- en bewegingsstoornissen die met stotteren geassocieerd zijn.

2 jaar geleden werd in een Belgisch onderzoek een rapportage gedaan over een ernstige stotteraar waarbij zijn stotteren heel erg verbeterde na eenmalige inname van methylfenidaat. Methylfenidaat is een stof die in België wordt geproduceerd onder de naam Rilatine®. Deze stof verhoogt de hoeveelheid beschikbare dopamine in de hersenen en zou dus de effecten van het stotteren kunnen tegengaan.

Met deze studie willen we onderzoeken of de inname van de stof methylfenidaat de ernst van het stotteren ook kan verminderen bij een grotere groep proefpersonen of dit enkel het geval was bij die ene persoon uit die Belgische studie van 2 jaar geleden. Er is evenwel geen enkele garantie dat uw deelname aan deze studie u voordeel zal opleveren.

Voordat u beslist over uw deelname aan deze studie willen we u wat meer informatie geven over wat dit betekent op organisatorisch vlak en wat de eventuele voordelen en risico's voor u zijn. Zo kan u een beslissing nemen op basis van de juiste informatie. Dit wordt "geïnformeerde toestemming" genoemd.

Wij vragen u de volgende pagina's met informatie aandachtig te lezen. Hebt u vragen, dan kan u terecht bij de arts-onderzoeker of zijn of haar vertegenwoordiger.

De studie wordt opgezet bestaande uit vrijwilligers en is een dubbel blinde placebo gecontroleerde studie. De deelnemer neemt eenmalig een dosis van 20mg methylfenidaat en eenmalig een placebo (een pilletje die geen actieve werkzame stof bevat). Tussen deze 2 eenmalige innames zit een periode van 2 weken. De duur van het onderzoek bedraagt 2 keer 1 dag. Alle deelnemers worden at

random in een van de 2 groepen verdeeld. Ook de onderzoeker weet op dat moment niet of u een placebo of methylfenidaat hebt gekregen. Dit gebeurt om geen vooroordelende houding te hebben tijdens het onderzoek. Er zal aan u gevraagd worden om een tekst te lezen en spontaan te praten om de ernst van het stotteren te objectiveren voor en 3u na inname van het pilletje. Tevens zal er gevraagd worden te antwoorden op enkele vragen. Uw deelname is vrijwillig; er kan op geen enkele manier sprake zijn van dwang. Voor deelname is uw ondertekende toestemming nodig. Ook nadat u hebt getekend, kan u de arts-onderzoeker laten weten dat u uw deelname wilt stopzetten.

Stopzetting van de deelname betekent simpelweg dat de deelnemer zijn "praktische" deelname stopzet omdat hij/zij de aan de studie verbonden verplichtingen te zwaar vindt, de bijwerkingen te onaangenaam vindt enz.

De deelname kan ook door de arts-onderzoeker worden stopgezet om veiligheidsredenen (evolutie van de ziekte) of andere redenen. Dit wil niet zeggen dat de deelnemer zijn/haar toestemming inzake de verzameling van aanvullende gegevens stopzet (indien hij/zij de arts-onderzoeker blijft bezoeken, die vaak ook zijn/haar referentiearts is voor de ziekte die in het kader van de klinische studie wordt behandeld).

Intrekking van de toestemming tot de studie betekent dat de deelnemer zijn/haar toestemming tot deelname aan de studie effectief intrekt. Dit kan zonder opgave van redenen en het kan betekenen dat de deelnemer zijn/haar toestemming inzake de verwerking van zijn/haar gezondheidsgegevens intrekt.

De gegevens die in het kader van uw deelname worden verzameld, zijn vertrouwelijk. Bij de publicatie van de resultaten is uw anonimiteit verzekerd.

De testen en het project staan onder toezicht van een arts van de vakgroep Huisartsgeneeskunde van de Vrije Universiteit Brussel. De verzamelde gegevens zullen opgeslagen worden in een databank waarbij uw persoonlijke basisgegevens niet in die databank terug te vinden zijn. De Vrije Universiteit Brussel heeft een verzekering aangegaan welke gebeurlijke schade voortvloeiend uit het onderzoek dekt.

Er worden u geen kosten aangerekend voor specifieke behandelingen, bezoeken / consultaties, onderzoeken in het kader van deze studie.

Proefpersonen moeten ouder zijn dan 18 jaar en lijden aan ontwikkelingsstoornissen. De proefpersonen mogen geen psychologische stoornissen zoals depressie, psychose of bipolaire stoornissen hebben. Ze mogen geen gediagnosticeerde ADHD, narcolepsie, leveraandoeningen of epilepsie hebben. Ook worden geen proefpersonen toegelaten die methylfenidaat gebruiken of in het verleden hebben gebruikt, een hoge bloeddruk hebben, zwanger zijn, borstvoeding geven en een of meerdere van de volgende medicatie gebruiken: benzodiazepines, neuroleptica zoals haloperidol, amphetamines, anti-emetica zoals metoclopramide en domperidone, L-dopa, MAO-inhibitoren. Proefpersonen met een voorgeschiedenis van glaucoom, CVA, TIA, medicatie-, alcohol- en drugsmisbruik worden eveneens niet toegestaan.

Tijdens het onderzoek worden op verschillende momenten de bloeddruk, temperatuur en de pols gemeten.

Alle geneesmiddelen hebben zowel bekende als onvoorspelbare bijwerkingen. Hoewel vroegere onderzoeken hebben aangetoond dat het studiegeneesmiddel die in het kader van deze studie wordt gebruikt, algemeen goed wordt verdragen, is het mogelijk dat u de hierna volgende bijwerkingen zal ondervinden.

Frequente: hoofdpijn, slaaploosheid, anorexie, emotionele instabiliteit, mogelijkheid tot misbruik.

Zeldzaam, vooral bij overdosering: psychotische reacties, compulsief gedrag, convulsies.

Indien u aan deze studie deelneemt, vragen wij u ten volle mee te werken voor een correct verloop van de studie en geen informatie over uw gezondheidstoestand, de geneesmiddelen die u gebruikt of de symptomen die u ervaart te verzwijgen.

Indien u besluit om aan deze studie deel te nemen, kan methylfenidaat al dan niet gunstig blijken te zijn voor de behandeling van ontwikkelingsstoornissen of het verminderen van de symptomen ervan.

De informatie, die dankzij dit onderzoek verkregen wordt, kan bijdragen tot een betere kennis van het gebruik van methylfenidaat of tot de ontwikkeling van een nieuw geneesmiddel voor de behandeling van ontwikkelingsstotteren bij toekomstige patiënten.

Als u bijkomende informatie wenst, maar ook ingeval van problemen of als u zich zorgen maakt, kan u contact opnemen met de arts-onderzoeker Prof. Dr. Dirk Devroey of een medewerker van zijn studieteam Rabaey Henk op het telefoonnummer (02/477.43.11 of ddevroey@vub.ac.be).

In geval van nood, kan u contact opnemen op het nummer 02/477.43.11.

Buiten de consultatie-uren moet u zich aanmelden op de spoedafdeling van uw ziekenhuis en vermelden dat u deelneemt aan een klinische studie. Uw dossier zal nuttige informatie bevatten voor de behandelde arts met betrekking tot de studie.

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Hoe kunnen wij u contacteren? -----

Ondergetekende,

stemt er mee in om deel te nemen aan het onderzoek met methylfenidaat en placebo bij volwassen ontwikkelingsstotteraars zoals hierboven beschreven.

Ik verklaar dat ik geïnformeerd ben over de aard, het doel, de duur, de eventuele voordelen en risico's van de studie en dat ik weet wat van mij wordt verwacht. Ik heb kennis genomen van het informatiedocument en de bijlagen ervan.

Ik heb voldoende tijd gehad om na te denken en met een door mij gekozen persoon, zoals mijn huisarts of een familielid, te praten.

Ik heb alle vragen kunnen stellen die bij me opkwamen en ik heb een duidelijk antwoord gekregen op mijn vragen.

Ik begrijp dat mijn deelname aan deze studie vrijwillig is en dat ik vrij ben mijn deelname aan

deze studie stop te zetten zonder dat dit mijn relatie schaadt met het therapeutisch team dat instaat voor mijn gezondheid.

Ik begrijp dat er tijdens mijn deelname aan deze studie gegevens over mij zullen worden verzameld en dat de arts-onderzoeker en de opdrachtgever de vertrouwelijkheid van deze gegevens verzekeren overeenkomstig de Belgische wetgeving ter zake.

- stemt er NIET mee in om deel te nemen aan het onderzoek met methylfenidaat en placebo bij volwassen ontwikkelingsstotteraars zoals hierboven beschreven.

Datum: .. / .. /

Handtekening van de deelnemer

.....

Zonder ondertekening van deze strook kan u niet deelnemen aan het onderzoek.