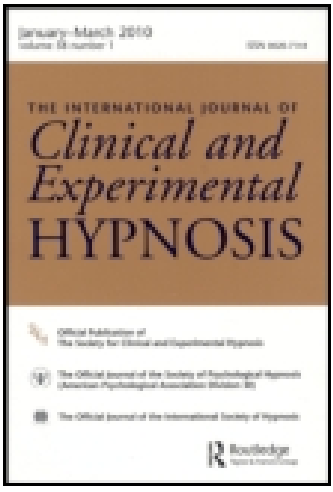

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METHYLPHENIDATE FACILITATES HYPNOTIZABILITY IN ADULTS WITH ADHD: *A Naturalistic Cohort Study*

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Abstract: Impaired attention may impede learning of adaptive skills in ADHD. While manipulations that reduce competition between attentional processes, including hypnosis, could boost learning, their feasibility in ADHD is unknown. Because hypnotic phenomena rely on attentional mechanisms, the authors aimed to assess whether stimulants could enhance hypnotizability in ADHD. In the current study, stimulant-naïve patients seeking treatment for ADHD-related symptoms were assessed with the Stanford Hypnotic Susceptibility Scale (SHSS) at baseline and during methylphenidate treatment. Methylphenidate dose and SHSS increase were negatively correlated with baseline SHSS scores. Upon reaching effective doses, mean SHSS scores increased significantly. All patients who had been poorly hypnotizable at baseline demonstrated moderate-to-high hypnotizability at follow-up. The data support methylphenidate enhancement of hypnotizability in ADHD, thus highlighting novel treatment approaches for this disabling disorder.

Attention deficit/hyperactivity disorder (ADHD) is a complex disorder characterized by high rates of comorbidity and social dysfunction (Kessler et al., 2006), with an estimated prevalence of 2.5% in adults (Simon, Czobor, Balint, Meszaros, & Bitter, 2009). ADHD has also been associated with maladaptive personality and coping strategies that limit the internal resources necessary for successful treatment (Young, Bramham, Gray, & Rose, 2008). Although diagnosis is often delayed until adulthood, even when treatment is begun during childhood, outcomes are relatively disappointing (Langley et al., 2010). Current guidelines recommend a multimodal approach for adults with ADHD that combines pharmacotherapy and psychotherapy (Kooij et al., 2010). While a dramatic increase in stimulant prescription was noted over

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the past decade (Olfson, Blanco, Wang, & Greenhill, 2013), research on psychological treatment of ADHD has been relatively modest. Nevertheless, recent studies suggest that the provision of psychological treatment in ADHD patients receiving stimulant therapy has an additive effect over medication alone (Emilsson et al., 2011). A recent systematic review on psychological treatment of ADHD in adults concluded that, although cognitive behavioral therapy may be effective, only a few controlled trials were published and further treatment modalities should be sought (Vidal-Estrada, Bosch-Munso, Nogueira-Morais, Casas-Brugue, & Ramos-Quiroga, 2012).

Hypnosis and hypnotherapy have been a major focus of investigation in recent years, not only with respect to psychiatric disorders but also for a vast array of medical fields, including pain disorders (Kisely, Campbell, Yelland, & Paydar, 2012), obstetrics (Madden, Middleton, Cyna, Matthewson, & Jones, 2012), oncology (Richardson et al., 2007), neurology (Senders, Wahbeh, Spain, & Shinto, 2012), and dentistry (Roberts, 2006), with significant therapeutic benefits noted in many of these conditions. Recently, hypnosis was demonstrated to facilitate specific learning modes by reducing competition between different attentional processes (Nemeth, Janacsek, Polner, & Kovacs, 2013). Based on these data, hypnotherapy could be assumed to help ADHD sufferers cope better with key daily life issues, for instance by enabling them to learn adaptive problem-solving strategies. Despite these potential merits, attempts to evaluate the efficacy of hypnotherapy for adults with ADHD have not been published to date, with only one small noncontrolled trial published relating to pediatric ADHD (Calhoun & Bolton, 1986).

The lack of trials assessing hypnotherapy for ADHD patients could be explained by the fact that, clinically, one would assume that clients with attentive disorders would not be very hypnotizable due to the fact that they have difficulty attending to hypnotic suggestions. Although not validated empirically, this impression seems logical, as hypnotic phenomena, by their definition, are largely dependent on attentional mechanisms. In fact, building on important contributions by researchers such as David and Herbert Spiegel (Spiegel & Spiegel, 2004), the Division 30 Executive Committee of the American Psychological Association (2014) has recently stressed in its official definition that "hypnosis is a state of consciousness involving focused attention" (para. 1). On the other hand, Barabasz and Barabasz found that children with ADHD were above average in hypnotizability (1996). Similarly, J. Kirsch and Sapp (2000) found that college students with extreme scores on inattention measures were also very hypnotizable. These empirical findings imply that hypnosis and hypnotherapy should not be ruled out a priori as a treatment option for adults with ADHD.

There is an emerging consensus that attention is elicited through a complex cerebral system presiding over a number of distinct neuronal circuits (Petersen & Posner, 2012; Posner & Petersen, 1990). Neuroimaging studies revealed that, during a conflict task, subjects with ADHD display distinct patterns of cortical activation compared to healthy controls (Bush et al., 1999). Moreover, findings from a follow-up study indicated that when adults diagnosed with ADHD are treated with stimulants, their activation patterns become similar to those of normal controls (Raz, 2005). Supporting this view, recent studies suggest a common mechanism of dopaminergic modulation affecting both attentional and hypnotic performance (Raz, 2005).

Based on the assumptions that potential benefits of hypnotherapy for adults with ADHD might be hampered by their low attention span and that stimulant treatment improves attention and possibly ameliorates core deficits in relevant neurocircuitry, we aimed to explore a role for methylphenidate (MPH) in facilitating hypnotizability among these patients. As published data concerning hypnotizability of adults with ADHD, either drug-naïve or medicated, are scarce, this pilot study employed a naturalistic cohort design, focusing on hypnotizability as the primary outcome measure, since this ability is a prerequisite for successful hypnotherapy.

Method

Setting and Participants

Our cohort was based on adult clients presenting to a university-affiliated general psychiatric outpatient clinic during the years 2009–2012. The clinic serves an adult population from diverse socioeconomic backgrounds and offers, among other services, a service of hypnotherapy for a variety of psychiatric disorders. Clients who expressed interest in this form of therapy underwent a full diagnostic psychiatric interview using the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed. [*DSM–IV–TR*]; American Psychiatric Association, 2000) as well as a routine assessment with the Stanford Hypnotizability Scale, Form C (SHSS:C; Weitzenhoffer & Hilgard, 1962), Hebrew version (Lichtenberg, Shapira, Kalish, & Abramowitz, 2009). Drug-naïve clients that were diagnosed with ADHD and were suffering from significant symptoms attributable to this diagnosis were offered a trial of stimulants. The study was approved by the local institutional review board.

Design

A cohort of 46 drug-naïve clients who met *DSM-IV-TR* criteria for ADHD without other comorbid Axis I diagnoses were prospectively

followed in a naturalistic manner over a mean period of 12 weeks (range = 7–15 weeks). Following administration of the SHSS:C, a short-acting MPH preparation was started at 10 mg twice daily and then titrated upwards based on clinical response, reaching a mean daily dose of 44.4 ± 15.7 mg (range = 20–80 mg) delivered once daily as a long-acting or extended-release preparation. Following the titration period, SHSS:C was re-administered. Subjects still requiring hypnotherapy at this time point were provided with the treatment.

Outcome Measures

The SHSS:C is a 12-item test, individually administered according to a standardized procedure (Hilgard, 1965). This scale has standardized norms and has proved relatively stable over time (Piccione, Hilgard, & Zimbardo, 1989). Some items on the SHSS:C evaluate response to direct suggestions, while others test for a loss or inhibition of motor control. Using objective behavioral criteria, each of the 12 items is scored pass-fail. Passing an item gives 1 point, so the total score on the SHSS:C ranges from 0 to 12. As administration of a Hebrew version of the SHSS:C to 169 subjects in Israel yielded comparable scores to the original English version as well as to other translated versions (Lichtenberg et al., 2009), the Hebrew version was used throughout this study. All testing was administered by the same psychiatrist, who was unaware of previous test scores until the last respondent was tested.

Statistics. Comparisons between SHSS:C scores at baseline and follow-up were determined by the student-paired *t* test. Relationships between SHSS:C scores and other variables were determined using Pearson's or Spearman's correlations. Dichotomous variables were assessed with a Pearson chi-square test. Bonferonni's correction for multiple testing was applied.

Results

Twenty-eight (61%) of 46 clients were male. Mean age was 31.6 ± 6.4 years (range = 19–44). Twenty-eight clients (61%) had an academic-level education. Mean SHSS:C score at baseline was 5.43 ± 1.91. Baseline SHSS:C score was not significantly correlated with gender ($p = .90$), age ($p = .26$), or education level ($p = .33$). A negative correlation was noted between SHSS:C item number (i.e., order of an item on the scale) and percent of clients passing on that specific item ($r = -.60$, $p = .041$), meaning that clients tended to receive higher passing rates on items performed earlier during the scale (see Figure 1).

A significant negative correlation was found between baseline SHSS:C score and the mean daily dose of MPH prescribed ($r = -.72$,

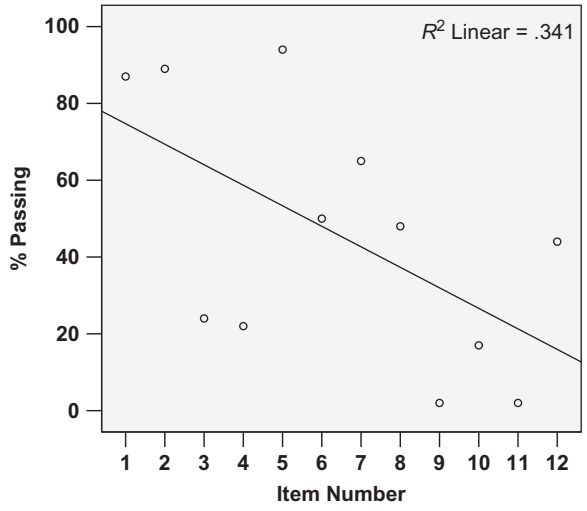

Figure 1. **Correlation between item number and percentage of clients passing on that specific item. A significant negative correlation between item number (i.e., position of an item during administration of the scale) and percentage of clients passing on that specific item is evident ($r = -0.595, p = .041$).**

$p < .001$), so that patients presenting with lower scores were generally titrated to higher doses of MPH (see Figure 2). Upon reaching effective MPH doses, SHSS:C was re-administered with a significant test-retest correlation coefficient ($r = .68$, $p < .001$). Mean SHSS:C score increased by 2.27 points compared to baseline (95% CI [1.83 to 2.70], $p < .001$, see Figure 3a). A correlation plot reduced to nine cells by grouping subjects into three scoring levels on the SHSS:C (high scores = 9–12; medium scores = 4–8; and low scores = 0–3) revealed a significant shift towards the higher hypnotizability score groups following MPH treatment ($p = .048$, see Figure 3b). Notably, all clients who had initially been low scorers received medium or high hypnotizability scores during MPH treatment.

A significant negative correlation between baseline SHSS:C score and the net SHSS:C increase following MPH treatment was noted ($r = –.59$, $p < .001$, see Figure 4), so that patients presenting with lower SHSS:C scores at baseline demonstrated larger SHSS:C improvements with MPH treatment. When entering demographic characteristics, MPH dose and baseline SHSS:C score into a regression model, the latter was found to be the only significant predictor of net SHSS:C increase

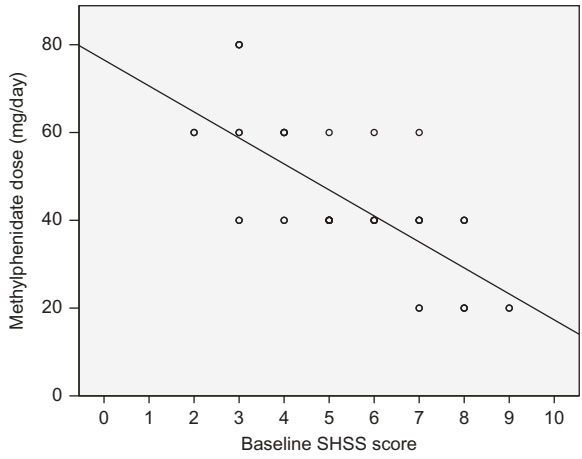

Figure 2. **Correlation between Stanford Hypnotic Susceptibility Scale, Form C (SHSS:C) scores at baseline and daily dose of methylphenidate (MPH) prescribed. A significant negative correlation between SHSS:C score at baseline and daily dose of MPH prescribed was noted ($r = -0.718$, $n = 46$, $p < .001$).**

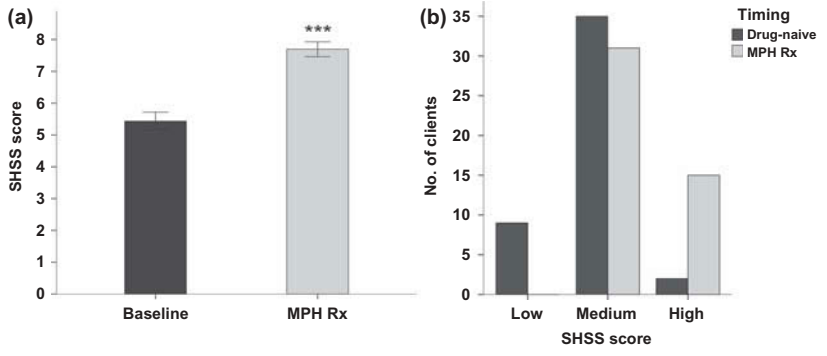

Figure 3. **Effect of methylphenidate (MPH) treatment on the Stanford Hypnotic Susceptibility Scale (SHSS) score. (a) Following treatment with MPH, a significant increase in total SHSS score was noted. (b) Number of clients with low, medium, and high hypnotizability scores at baseline (drug-naïve) and follow-up (MPH Rx). Notice that there were no clients with low hypnotizability scores at follow-up. ***$p < .001$.**

(net SHSS:C score improvement = 4.731 − 0.564 × [baseline SHSS:C score]). Examining changes in individual SHSS:C items revealed that, while the percent of clients passing on any specific item tended to improve following treatment with MPH, this improvement reached

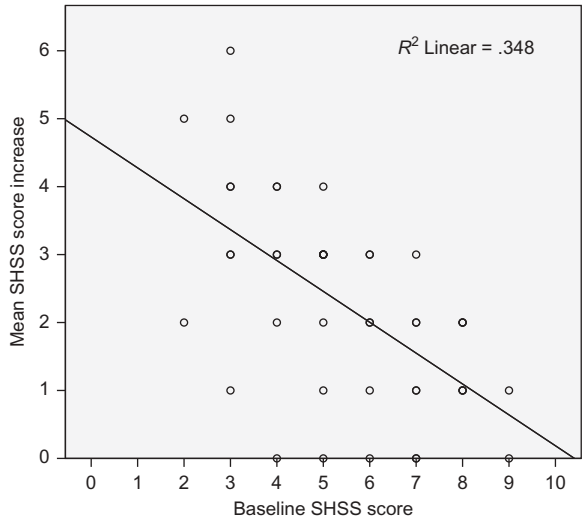

Figure 4. **Correlation between baseline Stanford Hypnotic Susceptibility Scale, Form C (SHSS:C) score and net increase at follow-up. A significant negative correlation between baseline SHSS:C score and net SHSS:C increase following methylphenidate treatment was noted ($r = -0.590, n = 46, p < .001$).**

statistical significance in four items (taste hallucination, arm immobilization, dream, and posthypnotic anosmia, see Table 1). The correlation between item number on the scale and item pass rates did not reach statistical significance during MPH treatment ($r = -.51$, $p = .089$).

Discussion

The data presented above reveal that, among ADHD clients, hypnotizability, as measured by the SHSS:C, significantly improved following treatment with MPH. Notably, lower SHSS:C scores at baseline were found to be a significant predictor of future improvement with MPH. We also demonstrated that lower SHSS:C scores at baseline predicted a prescription of higher MPH doses. Taken together, the current naturalistic data provide preliminary evidence for the efficacy of stimulant medications in improving hypnotizability among ADHD clients.

Table 1
Comparison of Positive Response Rate at Baseline and During MPH Treatment for Each SHSS Item

Item No.	Item description	% Positive on Item at Baseline	% Positive on Item During MPH Rx	*p* Value[a]
1	Hand lowering	87	98	*ns*
2	Moving hands apart	89	94	*ns*
3	Mosquito hallucination	24	33	*ns*
4	Taste hallucination	22	54	**.01**
5	Arm rigidity	94	98	*ns*
6	Dream	50	83	**.01**
7	Age regression	65	85	*ns*
8	Arm immobilization	48	87	**<.001**
9	anosmia	2	2	*ns*
10	Hallucinated voice	17	44	*ns*
11	Negative visual hallucination	2	11	*ns*
12	Posthypnotic anosmia	44	83	**<.001**

Note. Bold values represent significant differences.
[a]Significance level using Pearson chi-square with multiple testing correction.

Pharmacological attempts to improve hypnotizability in healthy population samples have been reported previously. For instance, studies that evaluated the acute effects of psychomimetics (Sjoberg & Hollister, 1965), cannabis (Kelly, Fisher, & Kelly, 1978), diazepam (Gibson, Corcoran, & Curran, 1977), and nitrous oxide (Whalley & Brooks, 2009) have yielded increases in hypnotizability ranging from 0.66% to 36%. However, to the best of our knowledge, this is the first published study that aimed to improve hypnotizability in a specific population of ADHD clients. The 2.27 point or 42% increase in total SHSS:C score that we observed during treatment with MPH translates into a large effect size of 0.84. This large effect size could be attributed, at least in part, to the fact that we treated ADHD clients with a drug that specifically targets some of the core deficits in this disorder. In this respect, the current study may offer a more personalized approach towards improving hypnotizability compared to the previous studies mentioned.

The large increase in total SHSS:C described above seems to be clinically meaningful, as it translates into a marked reduction in the number of poorly hypnotizable ADHD clients compared to their number prior to treatment. Notably, SHSS:C score at baseline was found to be the only significant variable in predicting score improvement during MPH treatment. As these variables were negatively correlated, the

maximal improvement in hypnotizability was obtained in those clients that might have otherwise gained little benefit from hypnotherapy. Given that some clinical uses of hypnosis and suggestion, such as pain relief, are known to be more effective in patients with higher susceptibility scores (Fricton & Roth, 1985), enhancing suggestibility of ADHD patients could allow hypnotherapeutic targeting of symptom domains such as social (dys)function (Langley et al., 2010), as well as quality of life (Goetz et al., 2012), that often respond only partially to stimulant therapy alone.

Although not compared directly in this study, the observed baseline hypnotizability score among ADHD patients does not seem to differ significantly from the commonly used norms, which are based on a sample of 533 Stanford University students (Hilgard, 1965). This finding is largely consistent with previous data demonstrating relatively high hypnotizability among clients with attention disorders (Barabasz & Barabasz, 1996; J. Kirsch & Sapp, 2000). Our finding regarding a progressive deterioration of item passing rates during administration of the hypnotizability scale, which was significant only before stimulant treatment, may imply that the decline in hypnotizability, rather than the overall scale score per se, may hamper the efficacy of hypnotherapy in these patients. This hypothesis is in accord with recent data suggesting that a shorter attention span may pose a major limitation to successful psychotherapeutic interventions in ADHD patients, especially when immediate reinforcement is unavailable (Vidal-Estrada et al., 2012).

In an attempt to delineate the attentional resources necessary for hypnotic responding, I. Kirsch, Burgess, and Braffman (1999) administered suggestions with and without cognitive load to high suggestible participants and low suggestible simulators. The data derived from these tests indicated that attentional resources were required for memory recall and memory suppression; however, their research also implied that various hypnotic suggestions such as challenge, ideomotor, and subjective experiences may also require variable attentional resources. Inferring from these findings, it seems highly plausible that pharmacological interventions that enhance attentional resources will have a positive effect on hypnotizability as well.

In addition to attentional resources, focused hypnotic concentration necessitates brain control over sensation and behavior. Thus, it is dependent on the interplay between executive control regions and the salience network. The latter network is involved in detecting, integrating, and filtering relevant somatic, autonomic, and emotional information. Accordingly, recent data demonstrated elevated functional coupling between the prefrontal cortex (PFC) and dorsal anterior cingulate cortex (dACC) in high compared with low hypnotizable individuals (Hoeft et al., 2012). Although ADHD patients typically display reduced connectivity between PFC and ACC (Peterson et al., 2009), a

recent review concluded that this deficit could be ameliorated by MPH treatment (Schweren, de Zeeuw, & Durston, 2013). Hence, MPH treatment may alter functional brain connectivity of ADHD patients in a specific direction that makes them more hypnotizable.

Although abundant data indicate that stimulant medications improve symptoms of inattention, notable variability exists in their optimal dosage. To date no consistent predictors of MPH-dose response in ADHD have been identified, although several genetic polymorphisms related to dopaminergic transmission have been associated with individual variability (Froehlich et al., 2011). In this respect, the finding that lower hypnotizability at baseline was correlated with higher doses of MPH treatment is intriguing. As MPH titration was based on clinical response, the sensitivity of the baseline SHSS:C score in predicting the final dose necessary to achieve adequate clinical response implies that hypnotizability may constitute an endophenotype within the spectrum of attention disorders.

A key feature of the current study lies in its naturalistic design, which is generally characterized by higher external validity (Levin, Louviere, Schepanski, & Norman, 1983). As it allows direct observation of clients in their usual treatment setting, its results could be generalized to a larger population of ADHD patients. Another important feature of the study is that it was designed in accordance with the Guidelines for Evaluating and Expressing the Uncertainty of NIST Measurement Results (Taylor & Kuyatt, 1994). By assuring that each client was evaluated by the same psychiatrist in the same location and under the same conditions, we were able to obtain a significant test-retest correlation coefficient of 0.68. This moderate test-retest correlation lies between a value of 0.90 obtained with next day retesting (Weitzenhoffer & Hilgard, 1959) and 0.60 for retesting that was performed 8 to 12 years later (Morgan, Johnson, & Hilgard, 1974). In this respect, the correlation that we observed seems to be satisfactory, as considerable variability in response to MPH is noted among adults with ADHD (Wilens, Morrison, & Prince, 2011). It is important to note that, although test-retest correlations could have been significant even though mean scores had changed in some consistent manner, SHSS is considered to be a stable measure over time, despite changes throughout life (Lifshitz, Cusumano, & Raz, 2013; Piccione et al., 1989). Therefore, it is less likely that the net increase in SHSS:C during stimulant treatment stems from the test-retest design we have used.

An important shortcoming of the study is the fact that measures pertaining to inattention, which might have been ameliorated by MPH treatment, could have mediated part of its favorable effect on hypnotizability. However, the current study aimed to provide preliminary evidence focusing on MPH facilitation of hypnotizability,

without dissecting its mechanism of action. Moreover, a defining feature of hypnosis is the flexibility it affords for modulating aspects of consciousness, rather than one particular state of attention that it induces (Lifshitz et al., 2013). To this end, future studies may reveal if MPH facilitates hypnotizability above and beyond its direct actions on attention.

In summary, our findings suggest that in addition to widely recognized beneficial effects of stimulant treatment in adult ADHD, hypnotizability may also be significantly enhanced with MPH. Moreover, our results suggest that this effect is more robust in individuals that would have been otherwise classified as poorly hypnotizable. Our data also suggest that as a measurable trait, hypnotizability may offer some predictive value for individual dose-response to stimulants. Although preliminary, these findings could have important clinical implications for the treatment of adults with ADHD. As current pharmacological interventions offer only partial amelioration of core symptoms, these patients could benefit from implementation of novel psychotherapeutic modalities. Future prospective randomized studies that include rigorous assessment of various ADHD symptom domains during hypnotherapy facilitated by MPH treatment are therefore eagerly warranted.

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Methylphenidat erleichtert die Hypnotisierbarkeit bei Erwachsenen mit AHDS: Eine naturalistische Kohortenstudie

Amit Lotan, Omer Bonne und Eitan G. Abramowitz

Abstrakt: Beinträchtigte Aufmerksamkeit kann bei ADHS das Erlernen adaptiver Fähigkeiten behindern. Während Manipulationen, inklusive Hypnose, die die Konkurrenz zwischen attentiven Prozessen reduzieren, das Lernen unterstützen können, ist ihre Umsetzbarkeit in bezug auf ADHS unbekannt. Da hypnotische Phänomene auf attentiven Mechanismen beruhen, versuchten die Autoren einzuschätzen, ob Stimulantien die Hypnotisierbarkeit bei ADHS verbessern könnten. In der aktuellen Studie wurden Teilnehmer zu Beginn der Studie und unter Methylphenidatbehandlung mittels Stanford Hypnotic Susceptibility Scale (SHSS) untersucht, die bis zum Zeitpunkt der Studie keine Stimulantien eingenommen hatten und wegen ihrer ADHS-Symptome in Behandlung waren. Die Methylphenidatdosis und die Zunahme im SHSS waren mit den baseline Daten des SHSS negativ korreliert. Mit Erreichen der effektiven Dosis stiegen die mittleren SHSS-Werte signifikant. Alle Patienten, die zu Beginn nur sehr schwer hypnotisierbar waren, zeigten moderate bis hohe Hypnotisierbarkeit im follow-up. Die Daten unterstützen die positive Wirkung des Methylphenidat in bezug auf die Hypnotisierbarkeit bei ADHS und somit neue Behandlungsansätze bei dieser sehr einschränkenden Erkrankung.

Stephanie Reigel, MD

Le méthylphénidate favorise l'hypnotisabilité chez les adultes souffrant du trouble d'hyperactivité avec déficit de l'attention (THADA) : l'étude naturaliste d'une cohorte

Amit Lotan, Omer Bonne et Eitan G. Abramowitz

Résumé: Le déficit d'attention peut nuire à l'apprentissage de compétences d'adaptation chez les personnes souffrant du THADA. Bien que les manipulations réduisant la compétition entre les processus attentionnels, y compris l'hypnose, puissent favoriser l'apprentissage, on n'en connaît pas la faisabilité dans le traitement du THADA. Les phénomènes hypnotiques étant fondés sur des mécanismes attentionnels, les auteurs ont cherché à déterminer si des stimulants pourraient augmenter l'hypnotisabilité chez les personnes atteintes du THADA. Dans le cadre de cette étude, des patients n'ayant aucune expérience des stimulants et cherchant un traitement de leurs symptômes liés au THADA ont répondu au Questionnaire de susceptibilité hypnotique de Stanford (SHSS) et leurs résultats ont été évalués au niveau de base et pendant le traitement au méthylphénidate. Les scores de base montraient une corrélation négative entre la dose de méthylphénidate et l'augmentation des résultats au SHSS. Toutefois, après l'atteinte des doses efficaces, les scores moyens augmentaient sensiblement. Les patients qui étaient faiblement hypnotisables au départ ont démontré une hypnotisabilité allant de modérée à élevée lors du suivi. Les données confirment par conséquent l'amélioration de l'hypnotisabilité

grâce au méthylphénidate chez les personnes souffrant du THADA, mettant ainsi en évidence des approches de traitement novatrices de ce trouble invalidant.

Johanne Reynault
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El metilfenidato facilita la hipnotizabilidad en adultos con TDAH: Un estudio naturalista de cohorte

Amit Lotan, Omer Bonne, y Eitan G. Abramowitz

Resumen: Una atención disminuida puede impedir el aprendizaje de habilidades adaptativas en personas con TDAH. Aunque algunas manipulaciones que reduzcan la competencia entre procesos atencionales, incluida la hipnosis, podrían incrementar el aprendizaje, su factibilidad con TDAH se desconoce. Dado que los fenómenos hipnóticos dependen de mecanismos atencionales, los autores buscaron evaluar si se puede aumentar la hipnotizabilidad con estimulantes en TDAH. En este estudio se evaluó a pacientes sin conocimiento de los estímulos que buscaban tratamiento para síntomas relacionados con TDAH, con la Escala Stanford de Susceptibilidad Hipnótica (ESSH) en la línea basal y durante el tratamiento con metilfenidato. La dosis del metilfenidato y el incremento en ESSH estuvieron negativamente correlacionados con las puntuaciones basales de la ESSH. Al alcanzarse dosis eficaces, la puntuación media de la ESSH incrementó significativamente. Todos los pacientes que habían resultado poco hipnotizables en la línea basal demostraron una hipnotizabilidad moderada a alta durante el seguimiento. Los datos sustentan el aumento en hipnotizabilidad por metilfenidato en TDAH, resaltando nuevos estrategias de tratamiento para este trastorno debilitante/

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