Psychological Medicine

cambridge.org/psm

Executive deficits in schizophrenia: mediation by processing speed and its relationships with aging

Flavien Thuaire[1], Fabien Rondepierre[2], Guillaume T. Vallet[1], Isabelle Jalenques[3] and Marie Izaute[1]

[1]Université Clermont Auvergne, CNRS, LAPSCO, 34 avenue Carnot – TSA 60401–63001 Clermont-Ferrand Cedex 1, Clermont-Ferrand, France; [2]Service de Psychiatrie de l'Adulte A et Psychologie Médicale, Centre Mémoire de Ressources et de Recherche, CHU Clermont-Ferrand, Clermont-Ferrand, France and [3]Service de Psychiatrie de l'Adulte A et Psychologie Médicale, Centre Mémoire de Ressources et de Recherche, CHU Clermont-Ferrand, Institut de Psychiatrie-GDR 3557, Université Clermont Auvergne, Clermont-Ferrand, France

Original Article

Cite this article: Thuaire F, Rondepierre F, Vallet GT, Jalenques I, Izaute M (2022). Executive deficits in schizophrenia: mediation by processing speed and its relationships with aging. *Psychological Medicine* **52**, 1126–1134. https://doi.org/10.1017/S0033291720002871

Received: 8 January 2020
Revised: 11 June 2020
Accepted: 27 July 2020
First published online: 25 August 2020

Key words:
Adulthood; aging; executive functions; Miyake's model; processing speed; schizophrenia

Author for correspondence:
Marie Izaute,
E-mail: marie.izaute@uca.fr

Abstract

Background. Executive deficits are a core characteristic of schizophrenia. Yet, the origin of these impairments remains unclear as they may be caused by processing slowing. This issue is of particular interest for aging insofar as cognitive aging is also associated with a decline in executive functioning and a slowing of processing speed. As schizophrenia patients' life expectancy increases, a better understanding of the origin of older patients' cognitive deficits becomes essential so that healthcare can be adapted to suit them. This study aims to determine whether processing speed mediates how schizophrenia affects executive functions and whether these relationships are moderated by age.

Methods. Sixty-two schizophrenia patients (27 women) and 62 healthy comparison subjects matched for age (range: 18–76 years), gender and education performed neurocognitive tests to evaluate their executive functions (shifting, updating, inhibition and access) and processing speed.

Results. Processing speed mediated the effect of schizophrenia on the four specific executive functions, and age moderated this mediation for shifting, updating and access, but in different ways. Age moderated the effect of processing speed on shifting, the direct effect of schizophrenia on access, and both the effect of processing speed and the direct effect of schizophrenia on updating.

Conclusions. This research highlights the need to evaluate processing speed routinely during therapeutic follow-up, as it is easy and simple to assess and appears to be at the heart of the cognitive deficits in schizophrenia. Finally, processing speed abilities yield information about the evolution of cognition with aging in schizophrenia.

Introduction

Cognitive impairment is a core feature of schizophrenia and affects most cognitive domains (Heinrichs & Zakzanis, 1998; Mesholam-Gately, Giuliano, Goff, Faraone, & Seidman, 2009). Deficits appeared even before the onset of schizophrenia (Meier et al., 2014) and patients' decline in later life is strongly related to their functional competencies (Harvey, Parrella, White, Mohs, & Davis, 1999; Kalache et al., 2015). An important issue in the study of schizophrenia is that both executive functions (EFs) (Reichenberg & Harvey, 2007) and processing speed (PS) (Dickinson, Ramsey, & Gold, 2007) are impaired and that these deficits may affect other cognitive abilities. However, despite the increase in schizophrenia patients' life expectancy (Cohen et al., 2008; Lee et al., 2018), the course of cognitive impairment in late adulthood remains unclear owing to the lack of studies that investigate this particular issue (Herold, Schmid, Lässer, Seidl, & Schröder, 2017; Rajji & Mulsant, 2008), and because normal aging is also associated with cognitive decline (Cona, Arcara, Amodio, Schiff, & Bisiacchi, 2013; Verhaeghen & Cerella, 2002). However, knowledge is crucial for adapting treatments and cognitive remediation to older schizophrenia patients. Given that remediation programs are currently better suited to younger patients, they need to be adapted to the specificity of older patients (Wykes et al., 2009).

EFs allow adapting behavior to diverse situations (e.g. creating a plan, initiating its execution, persevering until completion). They also mediate our ability to organize our thoughts in a targeted manner (Jurado & Rosselli, 2007). In other words, they are regarded as higher-order cognitive processes supporting other areas of cognition and thus are widely used in everyday life. Although executive functioning covers broad concepts, the importance of considering some specific EFs is now well established. The common distinction proposed identifies

© The Author(s), 2020. Published by Cambridge University Press

CAMBRIDGE UNIVERSITY PRESS

three specific EFs, namely shifting, updating and inhibition (Miyake et al., 2000). Subsequently, Fisk and Sharp (2004) identified a fourth function, referred to as 'access', which reflects the efficiency of access to long-term memory and may be assessed with word fluency tests.

Executive deficits in schizophrenia are well established (Fioravanti, Bianchi, & Cinti, 2012). A more fine-grained analysis of these deficits revealed impairments in shifting, updating and inhibition (Chan, Chen, & Law, 2006; Donohoe, Corvin, & Robertson, 2006; Rabanea-Souza et al., 2016; Raffard & Bayard, 2012; Wongupparaj, Kumari, & Morris, 2015) as well as access (Rossell, 2006), even though there were some discrepancies concerning inhibition (Chan et al., 2010; Laurenson et al., 2015; Thuaire et al., 2020; Westerhausen, Kompus, & Hugdahl, 2011). Importantly, insofar as EFs are strongly linked to everyday life skills (McClure et al., 2007) and quality of life (Tolman & Kurtz, 2012) in schizophrenia, they are an important target area for cognitive remediation (Penadés et al., 2010).

Nevertheless, it remains unclear whether executive impairment in schizophrenia comes from an executive impairment *per se* or from low-order processes instead. Contrary to executive functioning, which is thought to be uniquely human (Luria, 1966) or at least specific to the most intelligent species, lower-order processes are less evolved as cognitive functions. Those such as PS are implicated in almost every cognitive process. Thus, complex operations need to process simple operations quickly in order to keep their product available (Salthouse, 1996). Consequently, PS and EFs share some mutual variance (Albinet, Boucard, Bouquet, & Audiffren, 2012) but tap into different processes. Indeed, some authors suggested that PS is the most important deficit in patients (Dickinson et al., 2007) and may mediate EFs impairments (Rodríguez-sánchez, Crespo-facorro, González-Blanch, Pérez-Iglesias, & Vázquez-barquero, 2007). Accordingly, it was shown in schizophrenia that PS contributed significantly to executive functioning (Raffard & Bayard, 2012), even when the executive tests used were not time-constrained (Ojeda et al., 2012). Yet, it is worth mentioning that PS does not account for all the deficits in EFs (Neill & Rossell, 2013), and its statistical control does not cancel out the deficits in all measures of EFs (Savla et al., 2011). Thus, the relationships between PS and EFs may be very complex, as PS seems to mediate some executive deficits, although the analyses conducted in previous studies were not designed as accurate tests for mediation. Moreover, as both EFs and PS declined severely in healthy aging and appear to play a distinctive role in explaining age-related deficits (Albinet et al., 2012; Lee et al., 2012), we surmised that participants' age would be a good criterion for supplementing our knowledge about this mediation.

Indeed, as EFs and PS are both impaired in healthy aging and in schizophrenia, some studies looked at whether these processes would show accelerated aging. Accelerated aging means that age effects would be greater in patients than in healthy participants. Some of the studies which examined this question in terms of executive functioning concluded in favor of the existence of accelerated aging (Fucetola et al., 2000; Herold et al., 2017), while others did not (Irani, Kalkstein, Moberg, & Moberg, 2011; Loewenstein, Czaja, Bowie, & Harvey, 2012; Stirling et al., 2003). To shed some light on these controversial results, in a previous article our team analyzed the performances of young, middle-aged and older schizophrenia patients and healthy comparison participants in neuropsychological tests assessing the four specific EFs (Thuaire et al., 2020). The results showed that accelerated aging was observed for shifting, and that access was impaired in older schizophrenia patients. However, updating and inhibition were not more affected by the pathology with aging. Similarly, studies about the effects of accelerated aging on PS in schizophrenia are conflicting. One study found accelerated aging in Trail-Making-Test Part A (TMT-A) and digit symbol (Loewenstein et al., 2012), whereas another found it in TMT-A but not digit symbol (Bowie, Reichenberg, McClure, Leung, & Harvey, 2008), and a third study showed no accelerated aging in TMT-A (Herold et al., 2017). It is therefore not clear from the literature whether aging increases executive deficits and/or the cognitive slowing of schizophrenia patients in comparison to healthy participants. In light of the results of our previous work (Thuaire et al., 2020) and studies showing a link between PS and EFs performance (Neill & Rossell, 2013; Raffard & Bayard, 2012; Savla et al., 2011), one possibility might be that PS mediates some EFs and that such mediation may have different strengths according to specific EFs. Moreover, aging may have different effects on this mediation as a function of specific EFs.

Thus, we set out to analyze our previous study further to determine which specific EFs are strongly mediated by PS because such knowledge will help remediation programs target the root causes of the executive deficits. We hypothesized that PS would mediate the four specific EFs but with different strengths. Moreover, we wanted to ascertain whether age could be a moderator of these mediation effects in order to help adapt remediation programs to strengths and weaknesses specific to older patients. According to our previous study showing increased deficits in older patients for shifting and access (Thuaire et al., 2020), we surmised that age would moderate this mediation only for these functions. This result lends further weight to the arguments in support of the specificity of schizophrenia aging and the need to adapt remediation programs to older patients (Wykes et al., 2009).

Methods and material

Participants

The present study involves the same participants as those recruited and described in our previous study (Thuaire et al., 2020).

This study was conducted in accordance with ethical standards and with the approval of the local ethics committees (EudraCT 2010-A00857-32 and PRI 2000, HUS N°2326). Before the investigation started, and after receiving a full explanation about the study, all the participants gave their informed consent in writing. They were 62 clinically-stable outpatients with schizophrenia recruited from the Psychiatric Departments of the University Hospitals. Patients with any current co-morbid neurologic or psychiatric disorder, including alcohol or substance abuse or dependence, were not included. Their psychiatric symptoms were assessed according to the Positive And Negative Symptoms Scale (PANSS, Kay, Fiszbein, & Opler, 1987). They were screened for anxiety and depression using the Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith, 1983). Verbal intelligence quotient (IQ) was evaluated using vocabulary and arithmetic tests taken from the Wechsler Adult Intelligence Scale, revised (WAIS-R, Silverstein, 1982). Patients received stable doses of psychotropic medication for at least 4 weeks. In addition, 62 healthy comparison participants matching the patients in terms of age, gender and education were recruited from the community. None of these participants had a known neurological or

https://doi.org/10.1017/S0033291720002871 Published online by Cambridge University Press

Table 1. Demographic characteristics of patients with schizophrenia and comparison participants (standard deviations shown in brackets).

	Schizophrenia patients $n = 62$	Comparison participants $n = 62$	*t*-test	*p* value
Men/women	35/27	35/27		
Age (years)	46.4 (15.7)	46.7 (15.6)	0.1	*ns*
Level of education	11.3 (2.9)	11.5 (2.7)	0.3	*ns*
PANSS total	68.8 (18.8)			
Positive score	14.5 (5.1)			
Negative score	18.5 (7.4)			
General psychopathology	33.9 (9.4)			
HADS A	7.8 (3.8)	5.6 (3.4)	3.4	<0.001
HADS D	6.4 (3.3)	3.8 (2.9)	4.8	<0.001
Verbal IQ	86.6 (15.6)	99.2 (15.5)	4.5	<0.001

PANSS, Positive And Negative Symptom Scale; HADS, Hospital Anxiety and Depression Scale; IQ, Intelligence Quotient.

psychiatric affliction or was currently suffering or had suffered in the past from alcohol or substance abuse or dependence. The age of the participants ranged from 18 to 76 years.

Table 1 presents the demographical, clinical and descriptive statistics of the group comparison data.

Material

EFs were assessed according to the framework proposed by Miyake et al. (2000), which distinguishes three specific EFs (shifting, updating and inhibition), with the addition of Fisk and Sharp (2004) for the efficiency of access to long-term memory. Two tests were used for each specific function, and a further two tests were also used to assess PS. See the supplement for a more detailed description of the tests.

The scores used in the analyses consisted of:

Shifting tasks

Plus-minus task (Jersild, 1927; Spector & Biederman, 1976): Participants had to switch between adding and subtracting 3 in respect of different numbers. The shift cost was calculated as the difference between the time taken to complete the third list and the average for the first and second lists: T3 – [(T2 + T1)/2].

Number-letter task (Rogers & Monsell, 1995): Participants had to switch between processing consonants and vowels. The shift cost was calculated in the same way as in the plus-minus test: T3 – [(T2 + T1)/2].

Updating tasks

N-back task: Participants had to remember and update in memory only the last three letters said by the experimenter to decide whether each new one was the same as one of the three previous letters. The score was the number of correct answers (hits and correct rejections).

Self-Ordered Pointing Task (Petrides & Milner, 1982): Participants had to update in memory the drawings they chose, in order not to choose them anymore. The score was the number of different drawings selected.

Inhibition tasks

Stroop color word task (SCWT, Stroop, 1935), card version: Participants had to inhibit word reading in order to name the color of the ink used for words depicting colors. To reduce the potential bias of patients' cognitive slowing, we used the interference score proposed by Li & Bosman (1996): (Baseline – color word)/Baseline.

Hayling sentence Completion Test (HSCT, Burgess & Shallice, 1996): Participants had to inhibit the final word of sentences and say aloud a word that was not linked in any way with either the sentence or final word. The scores were the time taken to complete Part B and the number of errors in Part B.

Access tasks

Verbal fluency: Participants had to say aloud as many words as they could according to a phonemic or semantic rule. Two verbal fluency tasks were assessed, namely phonemic fluency (Letter P) and semantic fluency (category 'animals'). The score was the number of correct words in 60 s.

Processing speed tasks

Digit copying test (Weschsler, 1989): Participants had to write down the digit matching a number according to a key. The score was the number of items correctly reported in 30 s. This time limit was chosen to reduce the impact of executive abilities and memory on performance (Knowles et al., 2015).

Letter comparison test: On a sheet of paper displaying pairs of X and O, participants had to decide whether each pair was identical or different and to tick the corresponding box. The score was the number of correct items in 30 s.

Data analyses

Data used in this article are available at: https://osf.io/ebn5a/

Not all of the participants completed all the tests: five failed to complete the plus-minus test (4%), one the n-back test (0.8%), and 10 the HSCT (8%). The missing data were replaced using Multiple Imputation by Chained Equations (Azur, Stuart, Frangakis, & Leaf, 2011). See Thuaire et al. (2020) for more details.

Z-scores were computed for each task, based on mean and standard deviation of all participants, after which the means were calculated between the two tests in each of the four executive domains (shifting, updating, inhibition and access) and PS, to create a composite index for these cognitive abilities[1].

https://doi.org/10.1017/S0033291720002871 Published online by Cambridge University Press

All analyses were run on SPSS Statistics 25 (IBM Corp, 2017), running the PROCESS script to test the mediation (Hayes, 2018). Mediation signifies that the effect of an independent variable (IV) on a dependent variable (DV) is at least partly driven by a mediator (M). Several effects are calculated by means of regression analyses: (*a*) is the effect of the IV on M; (*b*) is the effect of M on the DV when controlling for the effect of the IV; (*c*) is the **total effect** of the IV on the DV and is the sum of a **direct effect** (*c*') of the IV on the DV and an **indirect effect** ($a \times b$) which is the effect of the IV on the DV through M. As regression analyses cannot test the significance of the indirect effect ($a \times b$), the latter is tested using a bias-corrected bootstrapping approach ($n = 5000$ bootstrap samples (Preacher & Hayes, 2008)). Thus, if zero is not in the 95% confidence interval, we can conclude that the indirect effect is significantly different from zero. Moderated mediation means that a moderator (W) affects at least one path of the mediation relation. The effect of one variable on another may, therefore, be different according to the value of the moderator. Group (0 = Comparison participants, 1 = Schizophrenia patients) was the IV, PS was the mediator, age was the moderator, and the four specific EFs were entered as DVs in separate analyses. Thus, the total effect is the effect of schizophrenia on a specific EF without taking into account a possible effect of PS. The direct effect is the effect of schizophrenia on a specific EF after controlling for the effect of PS, and the indirect effect is the effect of PS on a specific EF after controlling for the effect of schizophrenia. Unstandardized coefficients (B) are reported in the analyses.

Results

Table 2 presents means and standard deviations on the five indices for schizophrenia patients and healthy comparisons participants.

online Supplementary Table S1 presents intercorrelations among all study variables. All variables were significantly correlated with each other, except Group with Age, Group with Inhibition, and Age with Access.

Mediation analyses

Figure 1 shows the results of the mediation analyses about the effect of schizophrenia on the four specific EFs through PS. Path (*a*) indicates that schizophrenia had a strong negative effect on PS. Path (*b*) shows that higher PS increases performance in the four EFs. Mediation ($a \times b$) was significant for the four EFs, indicating that PS mediated the four EFs. Total effects of schizophrenia on EFs (*c*) were significant for shifting, updating and access, whereas direct effects of schizophrenia controlling for PS (*c*') only remained significant for updating and access.

Moderated mediation analyses

Moderation on a mediation model may be present in three paths: on the effect of the IV on M (path *a*), on the effect of M on the DV when controlling for the effect of the IV (path *b*), and the direct effect of the IV on the DV (path *c*'). However, as, despite a significant deleterious effect of age on PS ($B = -0.029$, $p < 0.001$), there was no moderation effect of age on path *a* ($B = -0.010$, $p = 0.197$), further analyses focus only on paths *b* and *c*'. Figure 2 shows the significant moderation effects of age on the mediation of the effect of schizophrenia on shifting (Panel A), updating (Panel B) and Access (Panel C) through PS. As may be seen in Fig. 2, age moderated the mediation of schizophrenia on three out of the four EFs, but in different ways.

Table 2. Mean *z*-scores on the four indices of specific functions and on processing speed (standard deviations shown in brackets)

	Schizophrenia patients	Comparison participants
Shifting	−0.302 (0.844)	0.302 (0.414)
Updating	−0.404 (0.810)	0.404 (0.661)
Inhibition	−0.058 (0.876)	0.058 (0.600)
Access	−0.481 (0.886)	0.481 (0.666)
Speed	−0.553 (0.891)	0.553 (0.679)

Moderation by age of the mediation by speed of the group effect on shifting

Conditional process analyses using PROCESS macro revealed that only path *b* was significantly moderated by age ($B = 0.011$, $p = 0.002$). Thus, the effect of PS on shifting abilities is moderated by age in such a way that the effect of speed on shifting is greater in older participants. Therefore, schizophrenia patients, whose PS is slower, are more affected by age when it comes to shifting abilities. Online Supplementary Figure S1 shows the effects of age on shifting as a function of participants' PS.

Moderation by age of the mediation by speed of the group effect on updating

PROCESS showed that both paths *b* ($B = -0.011$, $p = 0.045$) and *c*' ($B = -0.022$, $p = 0.030$) were significantly moderated by age. Thus, concerning path *b*, the effect of PS on shifting abilities is less in older participants and, consequently, for schizophrenia patients, whose processing performance is lower, older patients' updating performance would be less affected than that of younger patients. However, a counterbalancing effect is observed on path *c*' as age increases the effect of schizophrenia on updating, leading older schizophrenia patients to record a lower updating performance. Taken together, the effects of age on paths *b* and *c*' offset each other and resulted in an absence of accelerated aging in schizophrenia patients (Thuaire et al., 2020). Online Supplementary Figure S2 shows that the direct effect of schizophrenia on updating is more negative with advancing years, whereas the indirect effect is less negative with age.

Moderation by age of the mediation by speed of the group effect on inhibition

The analysis failed to show any moderation effect of age on paths *b* ($B = 0.005$, $p = 0.237$) and *c*' ($B = -0.006$, $p = 0.403$). Thus, the mediation by PS of the effect of schizophrenia on inhibition is not moderated by age.

Moderation by age of the mediation by speed of the group effect on access

PROCESS analysis revealed a significant moderation effect on path *c*' ($B = -0.016$, $p = 0.045$). Thus, as shown in online

https://doi.org/10.1017/S0033291720002871 Published online by Cambridge University Press

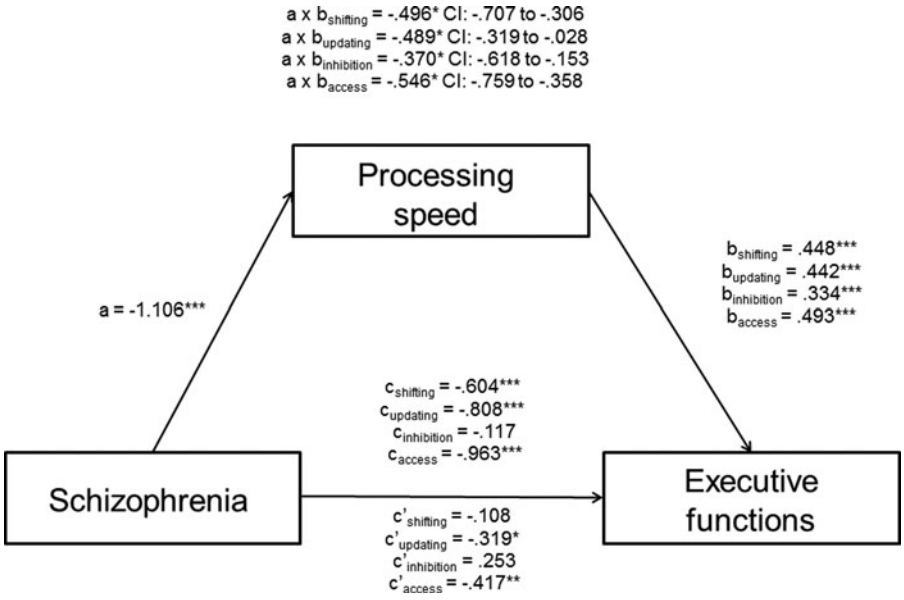


Fig. 1. Mediation model for the direct and indirect effects of schizophrenia on the four specific executive functions through processing speed. Numbers associated with *a*, *b*, *c*, *c'* and $a \times b$ are unstandardized regression coefficients. * $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$. CI = 95% bias-corrected bootstrap confidence interval.

Supplementary Figure S3, age moderated the direct effect of schizophrenia on access in a way that slowed the increase in schizophrenia patients' access performance with age.

Discussion

The first aim of this study was to test the mediating role of PS on the effect of schizophrenia with respect to the four specific EFs, namely shifting, updating, inhibition and access. The second aim was to determine how age affected this mediation as a function of the four specific EFs.

Concerning the first goal, our results confirm the widely observed cognitive slowing in schizophrenia (Dickinson et al., 2007; Leeson et al., 2010; Mesholam-Gately et al., 2009; Neill & Rossell, 2013; Ojeda et al., 2012; Savla et al., 2011) and the effect of PS on EFs (Rose, Feldman, & Jankowski, 2011; Salthouse, Fristoe, McGuthry, & Hambrick, 1998). Moreover, in accordance with the hypothesis that improving PS should bring widespread benefits in other cognitive functions (Cassetta & Goghari, 2016), PS mediates the effect of schizophrenia on EFs (Neill & Rossell, 2013; Ojeda et al., 2012; Savla et al., 2011). This result is consistent with Salthouse's Processing Speed Theory (Salthouse, 1996) and suggests PS should be efficient at successfully executing simple cognitive operations and keeping the result available for more complex operations such as cognitive strategies. Thus, fast processing may help to bear in mind current rules for shifting tasks, to switch faster between these rules, to update memory faster so that materials are not forgotten, to inhibit prepotent responses faster in order to activate an alternative response, and to activate and use efficient strategies to access memory.

With respect more specifically to mediation strength, shifting seems to be the specific EF mediated mainly by PS as it is the only one that showed significant total and indirect effects and no direct effect. The effect of schizophrenia on shifting is thus almost entirely the consequence of cognitive slowing. These results are in line with those of other studies which assessed shifting with the Wisconsin Card Sorting Test (Ojeda et al., 2012) or D-KEFS (Neill & Rossell, 2013; Savla et al., 2011). Our results also indicate that updating and access showed the most important total effect of schizophrenia, and both the direct and indirect effect remained significant, indicating that PS mediated most of the effect of schizophrenia on these EFs.

Finally, the mediation effect of schizophrenia on inhibition through PS is more complicated insofar as the total effect was not significant. According to Haye's Framework and contrary to Baron and Kenny's method (Baron & Kenny, 1986), a significant total effect is not required to test for mediation. More precisely, our result seems to be due to the opposite signs of the direct and indirect effects (Hayes, 2018). Thus, schizophrenia would seem to have a weak (and non-significant) positive direct effect (which is in keeping with both Baron and Kenny's and Haye's methods) on inhibition and a stronger negative indirect effect through PS. As the total effect is the sum of both direct and indirect effects (Hayes, 2018), the result is a non-significant total effect. This result warrants further research, but it is possible to speculate that if schizophrenia patients were not cognitively slowed their performances would be similar to comparison participants and even slightly better. Nevertheless, our results are in keeping with those observed with the D-KEFS in showing that PS contributed significantly to inhibition (Neill & Rossell, 2013; Savla et al., 2011).

The second aim was to determine whether age could be a moderator of this mediation effect as a function of the four specific EFs. Our main finding is that age moderated the mediation on three out of the four EFs, namely shifting, access and updating, albeit in different ways. According to a previous study (Thuaire et al., 2020) which showed that with respect to shifting and access schizophrenia patients were more affected by age than comparison participants, we postulated that the mediation effect on these EFs would be moderated by age. Our results supported this hypothesis and contributed to furthering knowledge about how age affects these functions in schizophrenia. Thus, the effect of PS on shifting was greater in older participants, suggesting that, compared with slower participants, faster participants may benefit from age as regards shifting. Yet, schizophrenia patients whose PS was severely impaired saw their shifting performance decline with age compared to healthy subjects, a result interpreted as accelerated aging (Thuaire et al., 2020).

https://doi.org/10.1017/S0033291720002871 Published online by Cambridge University Press

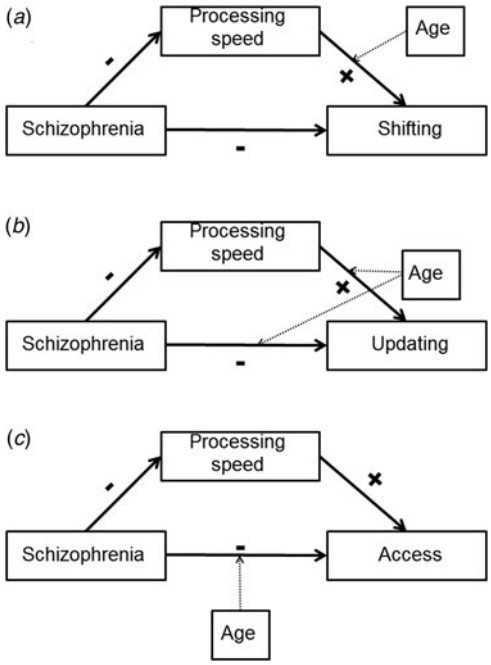


Fig. 2. Representation of the mediation of the effect of schizophrenia on executive functions through processing speed moderated by age for shifting (a), updating (b) and access (c).

With regard to access, the influence of age concerned the direct effect of schizophrenia and, as such, was independent of PS. More specifically, our results suggested that for comparison participants age was associated with an increase in access performance through the direct path, but that this was not the case for schizophrenia patients. The suggestion is therefore that it was the superior knowledge of vocabulary typical of healthy older adults (Fisk & Sharp, 2004) which was responsible for this increase in performance in the direct path. Moreover, where both groups were concerned, age affected the indirect path in the same way, namely through a slowing of processing which in turn reduced access performance. It is our suggestion that the two paths offset each other out for comparison participants, resulting in the absence of age effects (Fisk & Sharp, 2004), whereas for schizophrenia patients the direct path does not compensate for the indirect path. This interpretation of our results is in keeping with studies showing a greater age-related decline in verbal fluency in schizophrenia patients (Kosmidis et al., 2005; Thuaire et al., 2020). It is, therefore, possible that schizophrenia patients did not improve their vocabulary with aging as much as comparison participants, or that they failed to use effective strategies in both fluency tasks.

Surprisingly, and contrary to our hypothesis, mediation of the effect of schizophrenia on updating by PS was also moderated by age. However, an examination of the direct and indirect effects indicated that moderation of these effects had opposite signs and thus resulted in the absence of accelerated aging with respect to updating (Thuaire et al., 2020). More precisely, moderation of the direct effect showed that schizophrenia patients were more impaired in terms of updating as they got older. Conversely, moderation of the indirect effect indicated that the influence of PS on updating decreased with age. As schizophrenia patients' PS was slower, they were less affected by age on this path, which offset the effect of the direct path. These results suggest that older participants relied less on PS to complete these updating tasks than their younger counterparts. We presume they tried to compensate for their cognitive slowing by relying more on other processes such as working memory capacity or cognitive strategies, even if that was not enough for them to match the performance of younger participants (Thuaire et al., 2020). Such assumptions are in line with a meta-analysis of neuroimaging studies (Turner & Spreng, 2012), which showed that during an updating task older participants increased their recruitment of brain areas associated with learning and acquisition of cognitive strategies and cognitive control in working memory.

Finally, in keeping with our hypothesis and the fact that schizophrenia patients failed to show accelerated aging on inhibition (Thuaire et al., 2020), the mediation effect on this specific EF was not moderated by age.

These results suggest that PS should be assessed routinely during therapeutic follow-up and before including a patient in a remediation program. First, PS tasks are easy to administer and tap a central feature of the deficits in schizophrenia (Dickinson et al., 2007; González-Blanch et al., 2011). Second, since PS mediates EFs which are linked in turn to functional competencies (Harvey et al., 1999; Kalache et al., 2015), evaluating it may help to target other functions for investigation and third, aging may have different effects on patients' cognition depending on their PS. Specifically, lowest performance patients may show a major deterioration in shifting performance but relatively spared updating performance.

Moreover, our results also show the importance of the choice of pharmacological treatment. Long-term benzodiazepine use seems to have negative effects on several areas of cognition, including PS, even after withdrawal (Crowe & Stranks, 2018), and so it should be prescribed with caution. Concerning the treatment of depression, which is a comorbidity of schizophrenia, a meta-analysis showed that selective serotonin reuptake inhibitors had greater positive effects on cognition in depressed patients than the other classes of antidepressants (Prado, Watt, & Crowe, 2018). This result should be confirmed with further researches and tested in schizophrenia because it represents a possible area for improving patients' cognition. In any case, pharmacological treatment should be chosen and monitored so as to minimize neurocognitive side-effects, which may already be compromised by the disease process itself.

A potential implication of our results is that cognitive remediation programs should concentrate more on PS. Remediation programs targeting PS seem to be efficient (Garrido et al., 2013; Grynszpan et al., 2011; Lindenmayer et al., 2008; McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Sartory, Zorn, Groetzinger, & Windgassen, 2005; Vita et al., 2011). Thus, in light of our results showing that PS seems to underlie EFs, it is possible that increasing patients' PS would improve executive functioning (Rodríguez-sánchez et al., 2007).

This research has a number of strengths and limitations. First of all, EFs were assessed according to a validated model (Fisk & Sharp, 2004; Miyake et al., 2000) which depicts the diversity of EFs. Thus, our results lend further weight to arguments in favor of using specific models of executive functioning to study schizophrenia (Thuaire et al., 2020) insofar as we demonstrated how age affects the specific EFs differently through PS. Then, despite the numerous studies suggesting an underlying role for PS in the executive deficit in schizophrenia (Dickinson et al., 2007; Neill & Rossell, 2013; Ojeda et al., 2012; Raffard & Bayard, 2012; Rodríguez-sánchez et al., 2007; Savla et al., 2011), this article is

https://doi.org/10.1017/S0033291720002871 Published online by Cambridge University Press

the first to test this mediation with appropriate statistical analysis. Moreover, patients and comparison subjects were rigorously paired, one by one, for gender, age, and educational status. A recent meta-analysis (Fioravanti et al., 2012) indicated that the imbalance in the number of cases, gender composition and age could artificially increase between-group differences. However, we were unable to control former patients' medication or to clarify the long-term effects of medication on cognitive functioning. This may be a recurrent problem with cross-sectional studies on schizophrenia aging (Suzuki, Gen, & Inoue, 2011). Nonetheless, patients were treated in accordance with the guidelines for biological treatment of schizophrenia published by the World Federation of Societies of Biological Psychiatry (Hasan et al., 2012, 2013). They received stable doses of antipsychotics at least 4 weeks before inclusion and throughout the study, and most of the patients were administered only one antipsychotic which, presumably, would not cause the excessive cognitive deficit. Moreover, pharmaceutic research is making constant progress, and differences in treatments between younger and older patients not only affect current patients but will probably continue in the future too. The life expectancy gap between schizophrenia patients and the general population (Lee et al., 2018) makes it difficult to recruit patients over the age of 70, with the result that comparison participants were not as old as typically found in healthy aging studies. However, only longitudinal designs could overcome this limitation by keeping age pairing. Another recurrent limitation is that there is no pure measure of EFs or PS, and even symbol coding requires memory and executive functioning (Knowles et al., 2015). To reduce these biases, we aggregated two tasks for each function, and PS tasks were administered for 30 s to avoid the use of strategies or memory to perform them. However, it should be borne in mind that these cognitive processes are intrinsically linked, and it is still possible that, in combination with the model we tested, where PS mediates EFs, there is also a model where EFs mediate some PS performance.

Another statistical limitation concerns the use of psychometric assessment based on theory rather than statistics. However, the tests we used have a strong theoretical framework, and as cognition in schizophrenia patients differs from that of the general population it did not seem appropriate to us to calculate a principal component analysis.

In conclusion, this article is the first to show the mediation effect of PS on specific EFs with the help of a recent method that can be used to test the mediation directly (Hayes, 2018). Moreover, we showed that age affected the specific EFs through PS in different ways. These results have theoretical and clinical implications insofar as PS may explain various cognitive deficits in schizophrenia and should be a major target area for cognitive remediation. Several research studies have demonstrated the benefits of PS training (Garrido et al., 2013; Grynszpan et al., 2011; Lindenmayer et al., 2008; McGurk et al., 2007; Sartory et al., 2005; Vita et al., 2011). However, there is a need for remediation programs that specifically target PS with a view to defining how speed improvement transfers to other abilities (Cassetta & Goghari, 2016). Further research could test the hypothesis of a cascade model of cognition in schizophrenia, where PS impairment affects executive functioning, which, in turn, affects other cognitive processes, quality of life, and outcome. Another avenue for future research would be to complete our knowledge about relationships between cognitive processes in schizophrenia. For example, we could measure the contribution of attention, some components of which are impaired in schizophrenia. Indeed, top-down control of selective attention would appear to be impaired in schizophrenia, but not bottom-up control (Gold et al., 2018). Lastly, our results give indications for adapting cognitive remediation to suit older schizophrenia patients (Wykes et al., 2009) given that aging has a direct and stronger effect on updating and access in schizophrenia. However, there is no increased effect of age in patients with regard to inhibition and shifting, except through PS for the latter.

Supplementary material. For supplementary material accompanying this paper visit https://doi.org/10.1017/S0033291720002871

Acknowledgements. This work was supported by the CNRS, INSERM, the UCA of Clermont-Ferrand, and Clermont-Ferrand University Hospital. The authors would like to thank Elisabeth Bacon for her useful comments on a previous version of this article, Gillian Wakenhut for her accuracy and patience with correcting our English, and three anonymous reviewers for their helpful comments on the article. This project is co-funded by the European Union in the context of the European Regional Development Fund (ERDF) [Grant number AV0017611].

Conflicts of interest. None

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Note

1 For the inhibition score, we first computed a Z-score for HSCT which included time and errors before computing the inhibition score which included HSCT and SCWT, in order to give equal weight to both tests in the index. Where necessary, Z-scores were re-coded, so that a high score reflected better performance.

References

Albinet, C. T., Boucard, G., Bouquet, C. A., & Audiffren, M. (2012). Processing speed and executive functions in cognitive aging: How to disentangle their mutual relationship? *Brain and Cognition*, *79*(1), 1–11. https://doi.org/10.1016/j.bandc.2012.02.001.

Azur, M. J., Stuart, E. A., Frangakis, C., & Leaf, P. J. (2011). Multiple imputation by chained equations: What is it and how does it work? *International Journal of Methods in Psychiatric Research*, *20*(1), 40–49. https://doi.org/10.1002/mpr.329.Multiple.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social the moderator-mediator Variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, *51*(6), 1173–1182. https://doi.org/10.1037/0022-3514.51.6.1173.

Bowie, C. R., Reichenberg, A., McClure, M. M., Leung, W. L., & Harvey, P. D. (2008). Age-associated differences in cognitive performance in older community dwelling schizophrenia patients: Differential sensitivity of clinical neuropsychological and experimental information processing tests. *Schizophrenia Research*, *106*(1), 50–58. https://doi.org/10.1016/j.schres.2007.10.026.

Burgess, P. W., & Shallice, T. (1996). Response suppression, initiation and strategy use following frontal lobe lesions. *Neuropsychologia*, *34*(4), 263–272. https://doi.org/10.1016/0028-3932(95)00104-2.

Cassetta, B. D., & Goghari, V. M. (2016). Working memory and processing speed training in schizophrenia: Study protocol for a randomized controlled trial. *Trials*, *17*(1), 1–16. https://doi.org/10.1186/s13063-016-1188-5.

Chan, R. C. K., Chen, E. Y. H., & Law, C. W. (2006). Specific executive dysfunction in patients with first-episode medication-naïve schizophrenia. *Schizophrenia Research*, *82*(1), 51–64. https://doi.org/10.1016/j.schres.2005.09.020.

Chan, R. C. K., Huang, J., Guo, L., Cao, X., Hong, X., & Gao, Z. (2010). Executive control in schizophrenia in task involving semantic inhibition and working memory. *Psychiatry Research*, *179*(3), 259–266. https://doi.org/10.1016/j.psychres.2009.07.014.

Cohen, C., Vahia, I., Reyes, P., Diwan, S., Bankole, A., Palekar, N., … Ramirez, P. (2008). Schizophrenia in later life: Clinical symptoms and social well-being. *Psychiatric Services*, *59*(3), 232–234. https://doi.org/10.1176/ps.2008.59.3.232.

Cona, G., Arcara, G., Amodio, P., Schiff, S., & Bisiacchi, P. S. (2013). Does executive control really play a crucial role in explaining age-related cognitive and neural differences. *Neuropsychology*, *27*(3), 378–389. https://doi.org/10.1037/a0032708.

Crowe, S. F., & Stranks, E. K. (2018). The residual Medium and long-term cognitive effects of benzodiazepine Use: An updated meta-analysis. *Archives of Clinical Neuropsychology*, *33*(7), 901–911. https://doi.org/10.1093/arclin/acx120.

Dickinson, D., Ramsey, M. E., & Gold, J. M. (2007). Overlooking the obvious: A meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Archives of General Psychiatry*, *64*(5), 532. https://doi.org/10.1001/archpsyc.64.5.532.

Donohoe, G., Corvin, A., & Robertson, I. H. (2006). Evidence that specific executive functions predict symptom variance among schizophrenia patients with a predominantly negative symptom profile. *Cognitive Neuropsychiatry*, *11*(1), 13–32. https://doi.org/10.1080/13546800444000155.

Fioravanti, M., Bianchi, V., & Cinti, M. E. (2012). Cognitive deficits in schizophrenia: An updated metanalysis of the scientific evidence. *BMC Psychiatry*, *12*(64), 1471–1244. https://doi.org/10.1186/1471-244X-12-64.

Fisk, J. E., & Sharp, C. A. (2004). Age-related impairment in executive functioning: Updating, inhibition, shifting, and access. *Journal of Clinical and Experimental Neuropsychology*, *26*(7), 874–890. https://doi.org/10.1080/13803390490510680.

Fucetola, R., Seidman, L. J., Kremen, W. S., Faraone, S. V., Goldstein, J. M., & Tsuang, M. T. (2000). Age and neuropsychologic function in schizophrenia: A decline in executive abilities beyond that observed in healthy volunteers. *Biological Psychiatry*, *48*(2), 137–146. https://doi.org/10.1016/S0006-3223(00)00240-7.

Garrido, G., Barrios, M., Penadés, R., Enríquez, M., Garolera, M., Aragay, N., … Vendrell, J. M. (2013). Computer-assisted cognitive remediation therapy: Cognition, self-esteem and quality of life in schizophrenia. *Schizophrenia Research*, *150*(2–3), 563–569. https://doi.org/10.1016/j.schres.2013.08.025.

Gold, J. M., Robinson, B., Leonard, C. J., Hahn, B., Chen, S., McMahon, R. P., & Luck, S. J. (2018). Selective attention, working memory, and executive function as potential independent sources of cognitive dysfunction in schizophrenia. *Schizophrenia Bulletin*, *44*(6), 1227–1234. https://doi.org/10.1093/schbul/sbx155.

González-Blanch, C., Pérez-Iglesias, R., Rodríguez-Sánchez, J. M., Pardo-García, G., Martínez-García, O., Vázquez-Barquero, J. L., & Crespo-Facorro, B. (2011). A digit symbol coding task as a screening instrument for cognitive impairment in first-episode psychosis. *Archives of Clinical Neuropsychology*, *26*(1), 48–58. https://doi.org/10.1093/arclin/acq086.

Grynszpan, O., Perbal, S., Pelissolo, A., Fossati, P., Jouvent, R., Dubal, S., & Perez-Diaz, F. (2011). Efficacy and specificity of computer-assisted cognitive remediation in schizophrenia: A meta-analytical study. *Psychological Medicine*, *41*(1), 163–173. https://doi.org/10.1017/S0033291710000607.

Harvey, P. D., Parrella, M., White, L., Mohs, R. C., & Davis, K. L. (1999). Convergence of cognitive and functional decline in poor outcome schizophrenia. *Schizophrenia Research*, *35*, 77–84.

Hasan, A., Falkai, P., Wobrock, T., Lieberman, J., Glenthoj, B., Gattaz, W. F., … Möller, H. J. (2012). World federation of societies of biological psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, part 1: Update 2012 on the acute treatment of schizophrenia and the management of treatment resistance. *World Journal of Biological Psychiatry*, *13*(5), 318–378. https://doi.org/10.3109/15622975.2012.696143.

Hasan, A., Falkai, P., Wobrock, T., Lieberman, J., Glenthoj, B., Gattaz, W. F., … Möller, H. J. (2013). World federation of societies of biological psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, part 2: Update 2012 on the long-term treatment of schizophrenia and management of antipsychotic-induced side effects. *World Journal of Biological Psychiatry*, *14*(1), 2–44. https://doi.org/10.3109/15622975.2012.739708.

Hayes, A. F. (2018). *Introduction to mediation, moderation and conditional process analysis: A regression-based approach* (2nd Edn). New York: Guilford Press.

Heinrichs, R. W., & Zakzanis, K. K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology*, *12*(3), 426–445. https://doi.org/10.1037/0894-4105.12.3.426.

Herold, C. J., Schmid, L. A., Lässer, M. M., Seidl, U., & Schröder, J. (2017). Cognitive performance in patients with chronic schizophrenia across the lifespan. *GeroPsych*, *30*(1), 35–44. https://doi.org/10.1024/1662-9647/a000164.

IBM Corp. (2017). IBM SPSS Statistics for Windows, Version 25.0. IBM Corp.

Irani, F., Kalkstein, S., Moberg, E. A., & Moberg, P. J. (2011). Neuropsychological performance in older patients with schizophrenia: A meta-analysis of cross-sectional and longitudinal studies. *Schizophrenia Bulletin*, *37*(6), 1318–1326. https://doi.org/10.1093/schbul/sbq057.

Jersild, A. T. (1927). Mental set and shift. *Archives of Psychology*, *14*(Whole No 89), 5–82.

Jurado, M. B., & Rosselli, M. (2007). The elusive nature of executive functions: A review of our current understanding. *Neuropsychology Review*, *17*(3), 213–233. https://doi.org/10.1007/s11065-007-9040-z.

Kalache, S. M., Mulsant, B. H., Davies, S. J. C., Liu, A. Y., Voineskos, A. N., Butters, M. A., … Rajji, T. K. (2015). The impact of aging, cognition, and symptoms on functional competence in individuals with schizophrenia across the lifespan. *Schizophrenia Bulletin*, *41*(2), 374–381. https://doi.org/10.1093/schbul/sbu114.

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261–276. https://doi.org/10.1093/schbul/13.2.261.

Knowles, E. E. M., Weiser, M., David, A. S., Glahn, D. C., Davidson, M., & Reichenberg, A. (2015). The puzzle of processing speed, memory, and executive function impairments in schizophrenia: Fitting the pieces together. *Biological Psychiatry*, *78*(11), 786–793. https://doi.org/10.1016/j.biopsych.2015.01.018.

Kosmidis, M. H., Bozikas, V. P., Vlahou, C. H., Kiosseoglou, G., Giaglis, G., & Karavatos, A. (2005). Verbal fluency in institutionalized patients with schizophrenia: Age-related performance decline. *Psychiatry Research*, *134*(3), 233–240. https://doi.org/10.1016/j.psychres.2005.02.003.

Laurenson, C., Gorwood, P., Orsat, M., Lhuillier, J. P., Le Gall, D., & Richard-Devantoy, S. (2015). Cognitive control and schizophrenia: The greatest reliability of the stroop task. *Psychiatry Research*, *227*(1), 10–16. https://doi.org/10.1016/j.psychres.2015.03.004.

Lee, T., Crawford, J. D., Henry, J. D., Trollor, J. N., Kochan, N. A., Wright, M. J., … Sachdev, P. S. (2012). Mediating effects of processing speed and executive functions in age-related differences in episodic memory performance: A cross-validation study. *Neuropsychology*, *26*(6), 776–784. https://doi.org/10.1037/a0030053.

Lee, E. E., Liu, J., Tu, X., Palmer, B. W., Eyler, L. T., & Jeste, D. V. (2018). A widening longevity gap between people with schizophrenia and general population: A literature review and call for action. *Schizophrenia Research*, *196*, 9–13. https://doi.org/10.1016/j.schres.2017.09.005.

Leeson, V. C., Barnes, T. R. E., Harrison, M., Matheson, E., Harrison, I., Mutsatsa, S. H., … Joyce, E. M. (2010). The relationship between IQ, memory, executive function, and processing speed in recent-onset psychosis: 1-year stability and clinical outcome. *Schizophrenia Bulletin*, *36*(2), 400–409. https://doi.org/10.1093/schbul/sbn100.

Li, K. Z. H., & Bosman, E. A. (1996). Age differences in stroop-like interference as a function of semantic relatedness. Aging, *Neuropsychology, and Cognition*, *3*(4), 272–284.

Lindenmayer, J.-P., McGurk, S. R., Mueser, K. T., Khan, A., Wance, D., Hoffman, L., … Xie, H. (2008). A randomized controlled trial of cognitive remediation Among inpatients with persistent mental illness. *Psychiatric Services*, *59*(3), 241–247. https://doi.org/10.1176/ps.2008.59.3.241.

Loewenstein, D. A., Czaja, S. J., Bowie, C. R., & Harvey, P. D. (2012). Age-associated differences in cognitive performance in older patients with schizophrenia: A comparison with healthy older adults. *American Journal of Geriatric Psychiatry*, *20*(1), 29–40. https://doi.org/10.1097/JGP.0b013e31823bc08c.

Luria, A. R. (1966). *Higher cortical functions in Man*. New York: Basic Book.

McClure, M. M., Bowie, C. R., Patterson, T. L., Heaton, R. K., Weaver, C., Anderson, H., & Harvey, P. D. (2007). Correlations of functional capacity and neuropsychological performance in older patients with schizophrenia:

Evidence for specificity of relationships? *Schizophrenia Research*, *89*(1–3), 330–338. https://doi.org/10.1016/j.schres.2006.07.024.
McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *American Journal of Psychiatry*, *164*(12), 1791–1802. https://doi.org/10.1176/appi.ajp.2007.07060906.A.
Meier, M. H., Caspi, A., Reichenberg, A., Keefe, R. S. E., Fisher, H. L., Harrington, H., … Moffitt, T. E. (2014). Neuropsychological decline in schizophrenia from the premorbid to the postonset period: Evidence from a population-representative longitudinal study. *American Journal of Psychiatry*, *171*(1), 91–101. https://doi.org/10.1176/appi.ajp.2013.12111438.
Mesholam-Gately, R. I., Giuliano, A. J., Goff, K. P., Faraone, S. V., & Seidman, L. J. (2009). Neurocognition in first-episode schizophrenia: A meta-analytic review. *Neuropsychology*, *23*(3), 315–336. https://doi.org/10.1037/a0014708.
Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to Complex "Frontal Lobe" tasks: A latent Variable analysis. *Cognitive Psychology*, *41*(1), 49–100. https://doi.org/10.1006/cogp.1999.0734.
Neill, E., & Rossell, S. L. (2013). Executive functioning in schizophrenia: The result of impairments in lower order cognitive skills? *Schizophrenia Research*, *150*(1), 76–80. https://doi.org/10.1016/j.schres.2013.07.034.
Ojeda, N., Peña, J., Schretlen, D. J., Sánchez, P., Aretouli, E., Elizagárate, E., … Gutiérrez, M. (2012). Hierarchical structure of the cognitive processes in schizophrenia: The fundamental role of processing speed. *Schizophrenia Research*, *135*(1–3), 72–78. https://doi.org/10.1016/j.schres.2011.12.004.
Penadés, R., Catalán, R., Puig, O., Masana, G., Pujol, N., Navarro, V., … Gastó, C. (2010). Executive function needs to be targeted to improve social functioning with cognitive remediation therapy (CRT) in schizophrenia. *Psychiatry Research*, *177*(1–2), 41–45. https://doi.org/10.1016/j.psychres.2009.01.032.
Petrides, M., & Milner, B. (1982). Deficits on subject-ordered tasks after frontal- and temporal-lobe lesions in man. *Neuropsychologia*, *20*(3), 249–262.
Prado, C. E., Watt, S., & Crowe, S. F. (2018). A meta-analysis of the effects of antidepressants on cognitive functioning in depressed and non-depressed samples. *Neuropsychology Review*, *28*(1), 32–72. https://doi.org/10.1007/s11065-018-9369-5.
Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods*, *40*(3), 879–891. https://doi.org/10.3758/BRM.40.3.879.
Rabanea-Souza, T., Akiba, H. T., Berberian, A. A., Bressan, R. A., Dias, Á. M., & Lacerda, A. L. T. (2016). Neuropsychological correlates of remission in chronic schizophrenia subjects: The role of general and task-specific executive processes. *Schizophrenia Research: Cognition*, *3*, 39–46. https://doi.org/10.1016/j.scog.2015.12.001.
Raffard, S., & Bayard, S. (2012). Understanding the executive functioning heterogeneity in schizophrenia. *Brain and Cognition*, *79*(1), 60–69. https://doi.org/10.1016/j.bandc.2012.01.008.
Rajji, T. K., & Mulsant, B. H. (2008). Nature and course of cognitive function in late-life schizophrenia: A systematic review. *Schizophrenia Research*, *102*, 122–140. https://doi.org/10.1016/j.schres.2008.03.015.
Reichenberg, A., & Harvey, P. D. (2007). Neuropsychological impairments in schizophrenia: Integration of performance-based and brain imaging findings. *Psychological Bulletin*, *133*(5), 833–858. https://doi.org/10.1037/0033-2909.134.3.382.
Rodríguez-sánchez, J. M., Crespo-facorro, B., González-Blanch, C., Pérez-Iglesias, R., & Vázquez-barquero, J. L. (2007). Cognitive dysfunction in first-episode psychosis: The processing speed hypothesis. *British Journal of Psychiatry*, *191*(suppl 51), 107–110. https://doi.org/10.1192/bjp.191.51.s107.
Rogers, R. D., & Monsell, S. (1995). Costs of a predictable switch between simple cognitive tasks. *Journal of Experimental Psychology: General*, *124*(2), 207–231. https://doi.org/10.1037/0894-4105.20.6.675.
Rose, S. A., Feldman, J. F., & Jankowski, J. J. (2011). Modeling a cascade of effects: The role of speed and executive functioning in preterm/full-term differences in academic achievement. *Developmental Science*, *14*(5), 1161–1175. https://doi.org/10.1111/j.1467-7687.2011.01068.x.
Rossell, S. L. (2006). Category fluency performance in patients with schizophrenia and bipolar disorder: The influence of affective categories. *Schizophrenia Research*, *82*, 135–138. https://doi.org/10.1016/j.schres.2005.10.013.
Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological Review*, *103*(3), 403–428. https://doi.org/10.1037/0033-295X.103.3.403.
Salthouse, T. A., Fristoe, N., McGuthry, K. E., & Hambrick, D. Z. (1998). Relation of task switching to speed, age, and fluid intelligence. *Psychology and Aging*, *13*(3), 445–461. https://doi.org/10.1037/0882-7974.13.3.445.
Sartory, G., Zorn, C., Groetzinger, G., & Windgassen, K. (2005). Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. *Schizophrenia Research*, *75*(2–3), 219–223. https://doi.org/10.1016/j.schres.2004.10.004.
Savla, G. N., Twamley, E. W., Thompson, W. K., Delis, D. C., Jeste, D. V., & Palmer, B. W. (2011). Evaluation of specific executive functioning skills and the processes underlying executive control in schizophrenia. *Journal of International Neuropsychological Society*, *17*(1), 14–23. https://doi.org/10.1111/j.1743-6109.2008.01122.x.Endothelial.
Silverstein, A. B. (1982). Two-and four-subtest short forms of the Wechsler adult intelligence scale-revised. *Journal of Consulting and Clinical Psychology*, *50*(3), 415–418. https://doi.org/10.1037/0022-006x.50.3.415.
Spector, A., & Biederman, I. (1976). Mental Set and mental shift revisited. *American Journal of Psychology*, *89*(4), 669–679.
Stirling, J., White, C., Lewis, S., Hopkins, R., Tantam, D., Huddy, A., & Montague, L. (2003). Neurocognitive function and outcome in first-episode schizophrenia: A 10-year follow-up of an epidemiological cohort. *Schizophrenia Research*, *65*, 75–86. https://doi.org/10.1016/S0920-9964(03)00014-8.
Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, *18*(6), 643–662. https://doi.org/10.1037/h0054651.
Suzuki, H., Gen, K., & Inoue, Y. (2011). An unblinded comparison of the clinical and cognitive effects of switching from first-generation antipsychotics to aripiprazole, perospirone or olanzapine in patients with chronic schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *35*(1), 161–168. https://doi.org/10.1016/j.pnpbp.2010.10.021.
Thuaire, F., Rondepierre, F., Bacon, E., Vallet, G. T., Jalenques, I., & Izaute, M. (2020). Executive functions in schizophrenia aging: Differential effects of age within specific executive functions. *Cortex*, *125*, 109–121. https://doi.org/10.1016/j.cortex.2019.12.003.
Tolman, A. W., & Kurtz, M. M. (2012). Neurocognitive predictors of objective and subjective quality of life in individuals with schizophrenia: A meta-analytic investigation. *Schizophrenia Bulletin*, *38*(2), 304–315. https://doi.org/10.1093/schbul/sbq077.
Turner, G. R., & Spreng, R. N. (2012). Executive functions and neurocognitive aging: Dissociable patterns of brain activity. *Neurobiology of Aging*, *33*(4), 826.e1–826.e13. https://doi.org/10.1016/j.neurobiolaging.2011.06.005.
Verhaeghen, P., & Cerella, J. (2002). Aging, executive control, and attention: A review of meta-analyses. *Neuroscience & Biobehavioral Reviews*, *26*(7), 849–857. https://doi.org/10.1016/S0149-7634(02)00071-4.
Vita, A., De Peri, L., Barlati, S., Cacciani, P., Deste, G., Poli, R., … Sacchetti, E. (2011). Effectiveness of different modalities of cognitive remediation on symptomatological, neuropsychological, and functional outcome domains in schizophrenia: A prospective study in a real-world setting. *Schizophrenia Research*, *133*(1–3), 223–231. https://doi.org/10.1016/j.schres.2011.08.010.
Weschsler, D. A. (1989). *Echelle d'intelligence de Wechsler pour adultes forme révisée WAIS-R (ECPA)*.
Westerhausen, R., Kompus, K., & Hugdahl, K. (2011). Impaired cognitive inhibition in schizophrenia: A meta-analysis of the stroop interference effect. *Schizophrenia Research*, *133*, 172–181. https://doi.org/10.1016/j.schres.2011.08.025.
Wongupparaj, P., Kumari, V., & Morris, R. G. (2015). Executive function processes mediate the impact of working memory impairment on intelligence in schizophrenia. *European Psychiatry*, *30*(1), 1–7. https://doi.org/10.1016/j.eurpsy.2014.06.001.
Wykes, T., Reeder, C., Landau, S., Matthiasson, P., Haworth, E., & Hutchinson, C. (2009). Does age matter? Effects of cognitive rehabilitation across the age span. *Schizophrenia Research*, *113*, 252–258. https://doi.org/10.1016/j.schres.2009.05.025.
Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, *67*(6), 361–370. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x.

https://doi.org/10.1017/S0033291720002871 Published online by Cambridge University Press