Budapest University of Technology and Economics

PhD School in Psychology – Cognitive Science

AN EXAMINATION OF COGNITION AND CREATIVITY IN A DIMENSIONAL NEUROPSYCHIATRIC AND A PSYCHOPHARMACOLOGICAL FRAMEWORK

PhD thesis

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Glossary of abbreviations

ADH: attention-disordered and hyperactive

ADHD: attention-deficit/hyperactivity disorder

COMT: catechol-O-methyltransferase

DA: dopamine

DAT: dopamine transporter

DBH: dopamine beta-hydroxylase

fMRI: functional magnetic resonance imaging

ICD: impulse control disorder

LI: latent inhibition

LSD: lysergic acid diethylamide

MEG: magnetoencephalography

NRG1: neuregulin 1

O-LIFE: Oxford-Liverpool Inventory of Feelings and Experiences

PD: Parkinson's disease

PET: positron emission tomography

PFC: prefrontal cortex

SN: substantia nigra

SPQ: Schizotypal Personality Questionnaire

tDCS: transcranial direct current stimulation

VTA: ventral tegmental area

An examination of cognition and creativity in a dimensional neuropsychiatric and psychopharmacological framework

1. The dopaminergic systems from a cognitive neuroscience perspective

Dopamine (DA) is a catecholamine neurotransmitter involved in various functions of the central nervous system. In the brain, DA is produced by midbrain neurons of the substantia nigra (SN) and the ventral tegmental area (VTA). Dopamine can modulate neurotransmission through regulating the excitability of presynaptic neurons, through influencing the likelihood of vesicular neurotransmitter release evoked by action potentials, and through controlling qualitative and quantitative aspects of receptors in synapses (Tritsch & Sabatini, 2012). Midbrain DA neurons project to various subcortical (e.g. hippocampus, basal ganglia, amygdala, thalamus) and cortical targets. These projections were initially thought to form anatomically distinct dopaminergic pathways with separate functions: the nigrostriatal (or mesostriatal) pathway was suggested to be dominantly involved in motor control, the mesolimbic pathway was associated with motivation, the mesocortical pathway was implicated in cognitive control (Björklund & Dunnett, 2007), and the tubero-infundibular pathway was suggested to be responsible for regulating prolactin secretion (Hökfelt & Fuxe, 1972). It should be noted that in humans, the above outlined dopaminergic pathways turned out to be less segregated in terms of both structure and function (Düzel et al., 2009). In addition, there are DA neurons and DA receptors in the retina, which have been shown to be involved in light adaptation (Witkovsky, 2004). Five subtypes of dopamine receptors have been described so far, which belong either to the D1 (D1 and D5 subtypes) or to the D2 (D2, D3, and D5 subtypes) receptor families (Beaulieu & Gainetdinov, 2011). These receptor subtypes show different sensitivity to DA agonists and antagonists, which can enhance or block their function, respectively.

1.1 Motivational and cognitive functions associated with dopamine

The role of DA in motivation and cognitive control has been demonstrated by research from animal electrophysiology and pharmacology, and from human psychopharmacology and neuroimaging as well. In the following sections, we will discuss some of the key findings from these fields to illustrate how DA is implicated in these functions.

1.1.1 Dopamine plays a central role in reward processing

Dopamine neurons in the primate midbrain compute the **reward prediction error** (Schultz, Dayan, & Montague, 1997). That is, their phasic, burst-like activity is observed in

response to unexpected rewards and to unexpected cues predicting rewards. When an expected reward is omitted, these neurons show dips in their baseline tonic activity. These prediction error signals are assumed to modulate the updating of predictions in the projection targets of the midbrain DA neurons in order to make future behaviour more adaptive. Most midbrain DA neurons (70-80%) show the phasic, reward prediction error responses to unpredicted primary rewards, and a majority (60-75%) also responds to reward-predicting stimuli in a similar fashion. Curiously, a minority (10-15%) seems to be activated by both rewarding and aversive stimuli, which neurons' activity is thought to encode motivational salience (Schultz, 2013).

Moreover, the sustained activation of midbrain DA neurons measured between the presentation of a reward predicting cue and a reward has been found to encode **reward uncertainty**. That is, sustained tonic DA activation was the greatest after cues that predicted reward with a probability of 0.5, smaller for cues that were followed by rewards with probabilities of 0.25 and 0.75, while it was negligible after cues that perfectly predicted the delivery or the omission of a consequent reward (Fiorillo, Tobler, & Schultz, 2003). Tonic DA activation under reward uncertainty is assumed to boost learning about yet unknown but accurate predictors of reward.

These findings are paralleled by human functional neuroimaging works. For instance, a study that combined pharmacological manipulations with functional magnetic resonance imaging (fMRI) has revealed the involvement of the dopaminergic systems in learning from positive feedback (Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006). In this experiment, participants were given either haloperidol (a DA antagonist) or levodopa (precursor molecule of DA). Their behaviour and brain activity were measured while they performed an instrumental learning task which involved probabilistic monetary rewards and punishments. The pharmacological manipulation affected learning from reward: participants in the levodopa group won more money than participants in the haloperidol group. On the other hand, the two groups were comparable in terms of losses, so no effect of dopaminergic drugs on learning from punishment can be inferred from these results. Activity in the bilateral ventral striatum and the left posterior putamen mirrored computational estimations of reward prediction errors, while activity in the right anterior insula reflected computational estimations of punishment prediction errors. Importantly, reward prediction error-related activity in reward trials was modulated by the dopaminergic drugs.

The neural correlates of reward uncertainty have been examined in humans by Preuschoff, Bossaerts, and Quartz (2006). In their fMRI experiment, they systematically manipulated reward magnitude and reward uncertainty. They have found that expected reward

correlated linearly with immediate, stimulus-locked activation in the putamen and the ventral striatum. On the other hand, reward uncertainty correlated with delay period activation in the ventral striatum, the subthalamic nucleus, the midbrain, the mediodorsal thalamic nucleus, and the anterior insula. As these structures receive rich dopaminergic innervation, the authors argued that the measured activation is likely to indicate dopaminergic neurotransmission.

1.1.2 Dopamine is involved in cognitive control and flexibility

Dopamine's role in higher level cognitive control has been implicated by studies that examined **working memory** and executive functions. Animal studies have revealed the importance of prefrontal DA to working memory. For example, Sawaguchi and Goldman-Rakic (1991) injected a D1 antagonist into the prefrontal cortex (PFC) of rhesus monkeys, who were trained to perform a delayed oculomotor response task that measured visuospatial working memory. In this task, locations of target stimuli on the screen had to be remembered for few second long delays. The D1 antagonist impaired maintenance of visuospatial information during the delay, while it did not affect simple oculomotor control. A later study has shown that the relationship between prefrontal D1 activation and working memory-related neuronal firing is curvilinear; either too much or too little D1 activation in the PFC were found to be detrimental to working memory (Vijayraghavan, Wang, Birnbaum, Williams, & Arnsten, 2007).

Dopaminergic function of the PFC is not restricted to D1 receptors. On the basis of biologically informed computational work, it has been suggested that the prefrontal DA system can have two states, dominated by D1 or D2 DA receptor activation (Durstewitz & Seamans, 2008). In the D1-dominated state, the neural network system is unlikely to switch between different activity patterns, therefore it is characterised by robust representations, reduced distractibility, but decreased flexibility. To the contrary, in the D2-dominated state the neural network system can easily switch from activity pattern to another, thus it has increased flexibility, it is characterised by unstable representations, and in this state the system can demonstrate more spontaneous behaviour.

Cools and D'Esposito (2011) have added regional specificity to the above hypothesis. They based their model on a wide array of animal and human studies. According to their view, stabilising representations in working memory might depend on D1 receptor activation in the PFC, while flexible switching between representations might rely more on D2 receptor activation in the striatum, which is assumed to house a gating mechanism. The authors argued in favour of conceptualising cognitive **stability and flexibility** as two opposing and separate processes that may need to work together under certain circumstances.

1.1.3 Dopamine as the neuromodulator of exploration

Deyoung (2013) has recently suggested that DA might be the neuromodulator of **behavioural and cognitive exploration**. That is, DA could mediate the generation of new goals, strategies, and the search for novel patterns in the environment and in memory. From a cybernetic perspective, exploration has been defined as 'any behaviour or cognition motivated by the incentive reward value of uncertainty' (DeYoung, 2013, p. 2). While uncertainty obviously has aversive aspects and thus provokes anxiety (Hirsh, Mar, & Peterson, 2012), encountering uncertainty either physically or cognitively holds the promise of gains in knowledge. These gains can make uncertainty rewarding and attractive, in that approaching it can improve predictions and thus may lead to increased survival (DeYoung, 2013). This theory is supported by several lines of evidence. First, it has been shown that some DA neurons in the monkey midbrain respond not only to reward, but also to **novelty** (Schultz et al., 1997) and to any **salient** or **surprising** event, let it be reward or punishment (Matsumoto & Hikosaka, 2009). Furthermore, research with animals has revealed that DA-mediated changes in long-term potentiation underlie the beneficial effect of novelty on memory (Lisman & Grace, 2005). These effects are supported by a network which involves connections between the VTA, the hippocampus, the entorhinal cortex, the basal ganglia, and the PFC. Neuroimaging studies with humans have shown that activity in the SN/VTA is related to the processing of novel stimuli (Bunzeck & Düzel, 2006) and of cues that predict novelty (Wittmann, Bunzeck, Dolan, & Düzel, 2007). What is more, in an experiment where healthy participants were given a single dose of the DA precursor levodopa, magnetoencephalography (MEG) correlates of novelty processing in the mediotemporal lobe were found to be modulated by DA (Eckart & Bunzeck, 2013). Novelty processing was strikingly speeded up by levodopa: neural signature of discrimination between novel and familiar images was observed at around 150 ms post-stimulus in the levodopa group, whereas in the placebo control group it was detected later, between 600 and 1000 ms post-stimulus.

Shohamy and Adcock (2010) reviewed animal and human research that examined the role of DA in **motivational modulation of long-term memory**. The emerging picture indicated that DA signalling in the midbrain, associated with motivationally salient events such as rewards, novelty, surprise and effort, improve memory-related processes in the hippocampus. Dopaminergic modulation of hippocampal memories has been reported to occur under conditions where novelty or rewards are expected or encountered, and also under flexible encoding demands when multiple learning episodes need to be integrated. The authors of this review speculated that it might be more likely that tonic rather than phasic DA activation is

involved in such processes, but the available evidence did not allow firm conclusions. To sum up, the authors argued that dopaminergic neurotransmission biases memory towards motivationally relevant information, thus supporting adaptive behaviour in the future (Shohamy & Adcock, 2010).

1.2 Integration of creativity research with the cognitive neuroscience of dopamine

The way DA-mediated exploration was defined makes it fairly straightforward to connect it to the psychology of creativity. In the previous section, we have argued that DA has a major role in processing and approaching novelty, and ultimately supports adaptation to changed or unknown environments. As we shall see, novelty and adaptiveness are the cornerstones of creativity. Although creativity has enjoyed the attention of philosophers and psychologists for a long time, the lack of a strong conceptual foundation and the consequent methodological chaos have hindered the advance of creativity research (for the history of creativity definitions, see Runco & Jaeger, 2012), making creativity appear hardly available for neuroscientific research (Dietrich, 2004). Therefore, we will begin with elaborating on defining, conceptualising, and measuring creativity, then we will overview the differential psychology of creativity, and finally we will proceed to what cognitive neuroscience has revealed about dopaminergic brain mechanisms behind creativity.

1.2.1 Defining and measuring creativity

Creativity is the production of things that are novel and useful at the same time, according to the probably most widespread (Plucker, Beghetto, & Dow, 2004) and simplest definition, originally put forward by Stein (1953) and Barron (1955). However, the definition of creativity across different studies shows large variability. Plucker, Beghetto, and Dow (2004) examined the **definitions of creativity** in articles which were published in business, education, and psychology journals, or in two leading creativity journals. Strikingly, in the majority of the ninety papers they surveyed, creativity was not defined explicitly. Somewhat reassuringly, although they observed tremendous variation in the explicitly provided definitions of creativity, many of these definitions included uniqueness and usefulness as criteria of creativity. In their effort to help the field of creativity research progress, the authors of this review used content analysis to derive a comprehensive definition. Accordingly, they defined creativity as 'the interaction among *aptitude, process, and environment* by which an individual or group produces a *perceptible product* that is both *novel and useful* as defined within a *social context* [italics in original]' (p. 90). Expecting the field to agree in such an explicit definition might be overly

ambitious, the authors noted, but they recommended that researchers explicitly define creativity in publications in order to facilitate integration of the literature.

Importantly, a distinction can be made between **different levels of creativity**. Kaufman and Beghetto (2009) outlined four main levels where creativity can be investigated. First of all, Big-C stands for eminent creativity, and Big-C research focuses on creators whose products and ideas were very influential in a particular domain. Pro-c creativity refers to professional, expert but non-eminent creative achievements. The rationale behind the introduction of the Pro-c level is that whether one is a Big-C creator relies essentially on retrospective (and often posthumous) evaluations. Little-c creativity refers to everyday, naïve forms of creativity (e.g. decorating a room), while mini-c creativity is the emergence of new and personally meaningful interpretations inherent in learning. A virtue of this theory is that it improved precision of terminology in creativity research, and offered a useful framework to study the development of creativity. However, its application can be challenging, as instead of clear definitions it provided examples for each level.

Finally, it is important to consider that **creativity can occur in different domains**. For example, differences can be assumed between artistic and scientific creativity, which have been found to correlate with overlapping, but different sets of personality traits (see the meta-analysis of Feist, 1998). In line with this observation, it has been proposed that cognitive creativity might preferentially contribute to scientific discoveries and inventions in engineering, while affective creativity has been suggested to be beneficial to artistic expression and insights gained in psychotherapy (Dietrich, 2004). Evidence in favour of the domain-specificity of creativity additionally came from studies that found rather negligible correlations between the rated creativity of products created by the same participants in different domains, e.g. poetry, paintings, and stories (Baer, 1998; but see Silvia, Kaufman, & Pretz, 2009, for a critical perspective). Furthermore, principal component analysis of the Creative Achievement Questionnaire, a widespread self-report method assessing real life creative achievement in various domains, has yielded three components, each explaining a similar amount of variance (Carson, Peterson, & Higgins, 2005). Visual arts, writing, and humour loaded on the first component, representing expressive creative achievement. Dance, drama, and music loaded on the second component, which the authors named performative creative achievement. Last but not least, invention, science, and culinary arts loaded on the third component, which was labelled scientific creative achievement. Achievement in architecture did not have a relevant loading on any of these dimensions. In the same sample, a forced two component solution could explain smaller amount of variance, and yielded an art (drama, writing, humour, music, and

visual arts) and a science dimension (invention, science, and culinary arts). According to a more recent study, which applied latent class analysis, creative achievement appeared to be domain-specific, while self-description did not (Silvia, Kaufman, et al., 2009). In a university student sample, three latent classes emerged with respect to real life creative achievements, measured along objective criteria. Most people reported no achievements, whereas two minorities (each comprising around 17% of the sample) reported outstanding achievement either in visual arts or in performative arts (music, dance, writing, theatre, and film). To the contrary, subjectively defined creative self-descriptions across various domains did not form latent classes in another student sample, supporting domain generality for this aspect of creativity. Nevertheless, the idea of a domain general creativity factor is still appealing to several scholars (Chen, Himsel, Kasof, Greenberger, & Dmitrieva, 2006), and models that synthesise domain generality with domain specificity have been put forward (Baer & Kaufman, 2005; Plucker & Beghetto, 2004).

Complex theories of creativity offer a resolution to the debate surrounding the domain specific versus domain general nature of creativity. A prominent example is Amabile's componential model of creativity (1983), which described four stages of the creative process and separated the abilities that are related to a specific domain and to creativity in general. According to the model, the creative process begins with encountering a problem or a task. The next phase is preparation, where relevant information is searched for in the environment and in memory. In the following phase, possible responses are generated. Finally, the proposed ideas are tested against criteria and factual knowledge about the given domain. Importantly, the model listed three key components that may dominate different stages of the creative process: intrinsic motivation, domain-specific knowledge, and creative thinking skills. The latter component includes a cognitive style beneficial to creativity (e.g. breaking perceptual and cognitive sets, exploring new ideas, and suspending judgment), heuristics for coming up with novel ideas, concentration and persistence, and traits such as self-discipline and independence.

Divergent thinking can be placed under the broad umbrella term of creative thinking skills, as it involves coming up with novel ideas that break out of conventional frames of thought. Divergent thinking can be measured with simple tasks, thus it has been widely examined not only in psychology but also in cognitive neuroscience (Arden, Chavez, Grazioplene, & Jung, 2010; Dietrich & Kanso, 2010). Divergent thinking is the ability of coming up with multiple solutions to problems. It is frequently considered as an indicator of creative potential, i.e. a necessary but insufficient prerequisite of creativity achievement (Runco, 2008; Runco & Acar, 2012). In verbal divergent thinking tasks, participants are usually asked to list unusual uses for common objects, instances of common concepts, consequences

of fictional events, or similarities between common concepts (Silvia et al., 2008). In figural divergent thinking tasks, participants might be requested to finish an incomplete drawing (Urban, 2005) or to produce novel drawings that include simple pre-defined elements (Fugate, Zentall, & Gentry, 2013). Although many evaluating techniques have been proposed, four indices of divergent thinking dominate the literature. Fluency scores reflect the number of valid ideas, flexibility scores indicate the number of conceptual categories mobilised during ideation, and originality (or uniqueness) scores mirror the statistical infrequency of the ideas (Torrance, 1974). In addition, subjective scoring techniques have been developed, where the creativity of ideas and products generated by participants are rated by expert or naïve judges (Silvia et al., 2008). The external validity of divergent thinking test scores is supported by data showing that they correlate with concurrent real life creative achievement in adults (Carson et al., 2005) and scores on divergent thinking tests administered in childhood can predict real life creative achievement in young adulthood, even after controlling for the level of intelligence (Plucker, 1999). On the other hand, the excess reliance on single indices of divergent thinking in creativity research has received harsh criticism recently (see the debate between Baer, 2011a, 2011b; and Kim, 2011).

1.2.2 Differential psychology of creativity

Since the boom of psychometric creativity research in the middle of the 20th century (Guilford, 1950), a major line of studies focussed on how intra-individual factors (such as personality traits, intelligence, and executive control processes) relate to creative potential and achievements. In addition, several studies investigated how latent inhibition is associated with creativity. In the following section, we make an attempt to summarise the coherent findings, and also to illustrate some of the remarkable inconsistencies in the literature.

We start with a brief and selective overview of the literature about **personality traits associated with creativity**, focusing on key themes that are potentially relevant to our studies presented in this thesis. In their qualitative review of the earlier literature about the topic, Barron and Harrington (1981) have concluded that 'In general, a fairly stable set of core characteristics (e.g. high valuation of esthetic [sic!] qualities in experience, broad interests, attraction to complexity, high energy, independence of judgment, autonomy, intuition, self-confidence, ability to resolve antinomies or to accommodate apparently opposite or conflicting traits in one's self-concept, and, finally, a firm sense of self as "creative") continued to emerge as correlates of creative achievement and activity in many domains' (Barron & Harrington, 1981, p. 15). Later studies corroborated these findings. Important conclusions

emerged from a meta-analysis (Feist, 1998), which covered 83 studies investigating personality associated with eminent scientific or artistic creativity. Across various personality models and instruments, several personality traits had a consistently positive relationship with creative achievement. Among these were cognitive traits such as openness, flexibility, and imagination, motivational traits like impulsivity, ambition, and being driven, and several social traits ranging from self-confidence and autonomy through dominance to norm-doubting and hostility.

Probably the most comprehensive qualitative literature review about the differential psychology of creativity was published by Batey and Furnham (2006). After thoroughly and critically surveying the available literature, they concluded that openness is the most consistent predictor of creativity across various levels and domains. Some other traits were less consistently associated with creativity. For example, neuroticism appeared to be positively and remarkably associated with creativity in the arts, but negatively with creativity in science and in everyday situations. Interestingly, conscientiousness seemed to negatively predict artistic creativity, while it appeared to be highly beneficial to scientific creativity and, to a smaller extent, also to everyday creativity. Extraversion was positively related to everyday creativity, but negatively to eminent creativity in art and science.

Recently, the two meta-traits in the Big Five model of personality have been examined in relation to creativity (Silvia, Nusbaum, Berg, Martin, & O'Connor, 2009). Plasticity, consisting of openness and extraversion and thus thought to reflect tendencies towards behavioural and cognitive exploration, was consistently and positively related to various indicators of creativity, ranging from divergent thinking through everyday and empathic creativity to creative achievements. On the other hand, stability, encompassing agreeableness, conscientiousness, and reversed neuroticism was negatively related to everyday creativity but positively to empathic-social and math-science creativity. Interestingly, it has recently been suggested that individual differences in dopaminergic function might cause the shared variance of extraversion and openness, and thus predict variation in trait plasticity (DeYoung, 2013).

The **cognitive functions associated with creativity** may be classified along a simple dichotomy. A significant stream of studies emphasised that creativity demands focused and controlled attention, and high intelligence. On the other hand, a different line of research focused on spontaneous processes involved in creativity, and underscored the importance of defocused attention and uncontrolled associative thought in creativity (Beaty, Silvia, Nusbaum, Jauk, & Benedek, 2014). While the latter perspective tends to find commonalities between mental disorders and creativity, the former approach is more likely to discover factors that make a difference between the two (Fink, Benedek, Unterrainer, Papousek, & Weiss, 2014). First, we

discuss the association of creativity with intelligence and executive functions, two constructs involving controlled processing. Then, we focus on latent inhibition, a pre-attentive filter mechanism, whose disruption is has not only been linked to creativity but also to psychotic disorders.

How creative achievement and abilities are related to **intelligence** has been a central question in creativity research. After Guilford (1950) had stated that IQ tests are insensitive to some abilities that are crucial to creativity, psychometric research on creativity started to flourish, which involved the development of psychometric tests of creativity and related abilities. Initial research largely emphasised the independence of intelligence and creativity. For example, the seminal study of Getzels and Jackson (1962) formulated the threshold hypothesis, stating that intelligence and creativity are correlated only below a threshold of intelligence (around 120), above which no relationship can be found between the two. A recent study has corroborated the threshold hypothesis for indicators of creative potential (i.e. the number of ideas on divergent thinking tasks and their rated creativity), while it provided evidence for a weak linear relationship between creative achievement and intelligence (Jauk, Benedek, Dunst, & Neubauer, 2013). These results are in line with a qualitative literature review, which concluded that fluid and crystallised intelligence are rather related to creative achievement in science, while they are less associated with achievement in art and with creative potential (Batey & Furnham, 2006). Importantly, general intelligence is not only directly related to creative achievements, but also moderates the relationship between creative activities and achievements (Jauk, Benedek, & Neubauer, 2013). That is, higher intelligence might be useful when it comes to evaluating which creative activities are likely to be recognised by others, and also when others have to be convinced about the creative value of a product.

On the other hand, some have emphasised the independence of creativity and intelligence. For instance, a meta-analysis showed a weak but significant association (meta-analytic $r = 0.17$) between indicators of creativity and intelligence. The author of this study argued that this finding indicated that the relationship between creativity and intelligence is negligible (Kim, 2005). Ironically, another study that examined the association of IQ scores and divergent thinking scores found effects of similar magnitude and argued for the importance of intelligence in creative thinking (Silvia, 2008). These two examples nicely illustrate that the relationship between intelligence and creativity is still controversial and debated. More recent studies tend to focus on how specific indicators of creative potential and achievement are related to specific components of intelligence, such as broad retrieval ability (Silvia, Beaty, & Nusbaum, 2013) or crystallised intelligence (Beaty et al., 2014).

Likewise, several studies have attempted to map creative abilities and achievements to **executive functions.** Executive functions are higher level cognitive functions that regulate and organise lower level processes, thereby supporting goal-directed thought and action (N. P. Friedman & Miyake, in press). Most studies have shown that higher creativity is associated with more effective executive processes. For example, updating of representations in the 2-back task (Benedek, Jauk, Sommer, Arendasy, & Neubauer, 2014) and inhibition of prepotent responses in the Stroop task (Benedek et al., 2014; Edl, Benedek, Papousek, Weiss, & Fink, 2014) have both been shown to correlate with the production of creative ideas. On the other hand, a few studies have revealed that relaxation of certain components of cognitive control can also support creative thinking. For example, a study have found that inhibition of irrelevant memory representations correlated negatively with originality and fluency of divergent thinking (W.-L. Lin & Lien, 2013). Additionally, exhausting inhibitory control capacity with demanding executive tasks boosted fluency on a subsequent divergent thinking task and also increased indirect semantic priming. The latter finding suggests that loosened associative dynamics might mediate the beneficial effect of lowered inhibition on divergent thinking (Radel, Davranche, Fournier, & Dietrich, 2015). Finally, some authors have argued that the flexibility of cognitive control is essential to creativity. This line of reasoning is supported by a study that has shown that greater post-conflict control adjustments in the Stroop task are associated not only with higher level of creative potential (originality of divergent thinking) but with more creative achievements as well (Zabelina & Robinson, 2010). While these studies have emphasised the (flexibly) controlled nature of creative thinking, another segment of the literature has focussed on how creativity can rely on decreased attentional filtering, reflected by reduced latent inhibition.

Latent inhibition (LI) is the common and robust cross-species observation that repeated, non-reinforced pre-exposure of a stimulus inhibits later processing of that stimulus. Since the first report of LI in the goat in the late nineteen-fifties (Lubow & Moore, 1959), a definitive amount of research has been published on the neural, chemical, clinical and various other aspects of LI (Lubow, 2010). LI plays a crucial role in filtering out irrelevant information and it prevents the limited processing capacity from being overloaded; therefore, LI is essentially intertwined with mechanisms underpinning selective attention (Lubow, 2005).

Some studies have reported an association between LI and measures related to creativity. Higher real life creative achievement was associated with reduced or diminished LI in Harvard undergraduate samples with mean IQs near 130. Reduced LI and greater IQ were predictive of higher scores on the Creative Achievement Questionnaire (Carson, Peterson, &

Higgins, 2003). Moreover, reduced LI was associated with more original responses in a divergent thinking task, and with more pronounced creative personality traits. The above findings have been replicated and extended by Kéri (2011), who examined Hungarian participants recruited from the community, whose mean age was around 40 years and mean IQ was around 110. Similarly to the results of Carson and colleagues (2003), lower LI and higher IQ independently predicted lifetime creative achievements in this sample. Interestingly, the size of the primary, but not the broader social network positively predicted creative achievements, over and above the effects of LI and IQ. Although the study design did not permit drawing conclusions about the direction of causality, these results point toward the additive effects of cognitive and social factors in supporting creative achievement.

Conflicting results have been reported by another study that tested undergraduate students in the United Kingdom (sample mean IQ was ca. 110) and found that reduced LI was associated with reduced creativity (Burch, Hemsley, Pavelis, & Corr, 2006). It is important to note, that in this study, creativity was operationalised via a latent factor that had loadings from uniqueness scores of divergent thinking tasks, intelligence, creative self-descriptions, and openness. Differences in the methods used to measure LI and the sample characteristics might resolve the inconsistencies between the latter and the previously cited research findings.

Given that openness is consistently and robustly associated with various indicators of creativity (see e.g. Silvia, Nusbaum, et al., 2009), it is noteworthy that in a Harvard student sample with a mean IQ above 130, higher openness scores were associated with reduced LI (Peterson & Carson, 2000). This finding has been replicated in a different student sample, where lower LI was additionally associated with higher extraversion and self-reported creative personality traits (Peterson, Smith, & Carson, 2002).

At this point, it is important to consider that reduced LI has consistently been associated with acute and unmedicated, but not chronic and medicated schizophrenia (see the review by Kumari & Ettinger, 2010). In addition, an association of small-moderate effect size between reduced LI and (positive) schizotypy has frequently been reported. Some controversies exist in this literature, which might be related to comorbid drug abuse and smoking, differences in parameters of the LI experiments, and to the differential association between LI and different symptom dimensions. For example, reduced LI is a well-established animal model of the positive symptoms of schizophrenia (Lubow, 2005), while abnormally persistent LI has been proposed to be an animal model of the negative and cognitive symptoms of the disease (Weiner & Arad, 2009).

Additionally, reduced LI has been documented in adults diagnosed with attention-deficit/hyperactivity disorder (ADHD) only if they had taken their methylphenidate or amphetamine salt medication, which modulate the DA system. Normal LI has been documented in these patients at a second testing session when medication had been withdrawn since the morning of the very day of the experiment (Lubow, Kaplan, & Manor, 2012). In contrast, in boys with ADHD (age range: 8 – 15 years) who were methylphenidate-resistant and therefore had been drug-free for at least two months prior to the experiment, reduced LI was found for stimuli presented in the left visual hemifield. Normal LI was observed in these boys for stimuli appearing in the right visual field, and LI was normal for stimuli shown in either of the visual hemifields in boys with ADHD who were receiving methylphenidate treatment (Lubow, Braunstein-Bercovitz, Blumenthal, Kaplan, & Toren, 2005).

Before we start discussing evidence from cognitive neuroscience that implicated the dopaminergic modulation of creativity, it is important to see how focussing on trait-like individual differences is limited in providing a comprehensive picture of real life creativity. In his overview of shifts of focus in creativity research, Pléh (2010) emphasised that beyond characteristics tied to individuals (such as intelligence, openness, or divergent thinking ability), several other influences can be crucial to the fulfilment of creative potentials. Some examples include, but are not limited to the presence of mentors, the course of life stories, the capability to integrate diverse domains and the opportunity to contribute to a novel, developing (scientific) field, together with the cultural-historical milieu and the Zeitgeist. To sum up, although individual differences fostering creativity are well studied and undoubtedly relevant, it should be kept in mind that creation usually happens in a broader, social-cultural context.

1.2.3 Cognitive neuroscience of creativity

Neuroimaging research on creativity has been on the rise in the past two decades. We are not going to discuss this field of research in the detail, as comprehensive critical reviews (Arden et al., 2010; Dietrich & Kanso, 2010) and meta-analyses are available (Gonen-Yaacovi et al., 2013; Wu et al., 2015). Instead we will focus on studies that yielded findings that are highly relevant to the dopaminergic systems.

A study examined fourteen healthy middle-aged adults (mean age = 56 years) with positron emission tomography (PET) (de Manzano, Cervenka, Karabanov, Farde, & Ullén, 2010). Each participant was given a composite divergent thinking score reflecting their performance on figural, verbal, and numeric divergent thinking tasks. D2 receptor density in the thalamus was negatively correlated with this composite divergent thinking index, while D2

receptor density in the striatum or in the frontal cortex was not significantly associated with divergent thinking. The authors speculated that reduced thalamic D2 receptor density might lead to reduced thalamic gating thresholds and thus decreased filtering of information flow, ultimately leading to enhanced ideation in healthy participants. This study was limited by the small sample size, the specific age range, and a curiously long interval of eighteen months between psychological testing and the PET examination.

A different study that examined 52 healthy young adults in Japan applied voxel-based morphometry to assess the grey matter volume of structures with rich DA innervation, namely the dorsolateral PFC, the striatum, and the midbrain (Takeuchi et al., 2010). The authors found that the volumes of these structures were positively correlated with scores on a verbal divergent thinking test standardised for Japanese speakers. It should be highlighted that the study did not involve any DA-specific measurement, and the findings should be carefully extrapolated to participants from different cultures.

To sum up, neuroimaging research on creativity with relevance to the DA systems should be considered exploratory at its present state. However, two further major lines of evidence link creativity to DA: behavioural genetic studies and studies of patients with Parkinson's disease receiving DA therapy. We are going to overview research from the former field right here, while the latter is to be discussed in a later chapter.

Behavioural genetic studies have repeatedly reported that performance on divergent thinking tasks, indicating creative potential, were linked to polymorphisms of genes related to the dopaminergic systems. A study examining almost two hundred university students have linked polymorphisms of the DRD4 DA receptor gene with verbal and figural divergent thinking. Carriers of the 7-repeat variant of the DRD4 gene gave less ideas on the divergent thinking tasks, and their ideas came from fewer semantic categories (Mayseless, Uzefovsky, Shalev, Ebstein, & Shamay-Tsoory, 2013). Another exploratory behavioural genetic study tested nearly a hundred university students (Reuter, Roth, Holve, & Hennig, 2006). In this sample, the A1 variant of the DRD2 DA receptor gene was related to flexible, imaginative thinking and divergent problem solving. Polymorphisms of catechol-O-methyltransferase (COMT), an enzyme playing a key role in DA metabolism dominantly in the PFC, were not related significantly to any indicators of creative thinking skills in this study.

A different research group investigated the association of polymorphisms in the COMT DRD2, DRD4, TPH1, and the DA transporter (DAT) genes with divergent thinking in a sample of 147 university students (Runco et al., 2011). DAT and DRD4 polymorphisms were related to the quantity of ideas on a verbal divergent thinking task, while COMT, TPH1 and DRD4

polymorphisms predicted variance in the quantity of ideas in a figural measure of divergent thinking. In addition, DAT had a significant effect on flexibility scores, which indicate the number of different semantic categories mobilised during ideation. Originality of ideas was not significantly associated with any of the polymorphisms investigated in the study. Later, the authors reanalysed their data, and reported that several significant two- and three-way gene-gene interactions between the above listed DA genes were associated with originality and flexibility of verbally assessed divergent thinking (Murphy, Runco, Acar, & Reiter-Palmon, 2013). Sadly, the latter two reports did not report which variants of the listed genes predicted better divergent thinking.

Kéri (2009) investigated the association of the polymorphisms of the neuregulin 1 (NRG1) gene with creative potential and achievement in a sample of two hundred healthy adults (mean age = 35.5 years). It should be highlighted that the sample comprised highly intelligent participants (mean IQ = 124.7), who were eminent or creative in art or science. Other studies have shown that NRG1 regulated dopaminergic and glutamatergic neurotransmission (Newell, Karl, & Huang, 2013) and its T/T variant could predict risk for developing psychotic disorders (Hall et al., 2006; Kéri, Kiss, & Kelemen, 2009). According to the results of Kéri (2009), carriers of the T/T variant of the NRG1 gene exhibited greater lifetime creative achievement and had higher scores on a verbal divergent thinking task, relative to C/T carriers, who in turn were superior to C/C carriers in terms of creative potential and achievement as well. These results indicated that a genetic predisposition towards psychotic disorders (Hall et al., 2006; Kéri et al., 2009) might foster creativity in healthy people who possess outstanding intellectual abilities.

A more recent study examined dopaminergic gene-gene interactions in relation not only to divergent thinking, but also to real life creative achievements (Zabelina, Colzato, Beeman, & Hommel, 2016). The authors of this study argued that the COMT gene polymorphisms are related to PFC DA levels and efficiency of top-down control. Furthermore, they theorised that the DAT gene polymorphisms should be related to striatal DA function and cognitive flexibility. In one hundred young adults they found that different constellations of the variants of these two genes predicted divergent thinking and creative achievement. Carriers of the 9-repeat DAT variant (presumably associated with greater cognitive flexibility) who also carried the Val/Met COMT variant (putatively associated with mild top down control) have come up with highly original ideas on a divergent thinking task. Highly original ideas were also observed among carriers of the 10-repeat DAT variant (probably indicating low cognitive flexibility) who carried the Met/Met variant of the COMT gene (probably indicating strong top-down control). In case

of real life creative achievements, an essentially different pattern emerged. Carriers of the Val/Val variant of the COMT and 9-repeat variant of the DAT gene (assumed to have low cognitive flexibility and weak top-down control) reported the highest number of real life creative achievements. The authors concluded that creative ideas and achievements might supported by different cognitive styles, associated with variation in the above mentioned genes.

Although these explorative behavioural genetic studies consistently underlined the role of dopaminergic genes in creative thinking skills and creative achievement, more or less they all suffered from a significant limitation. The size of their samples were far below than what is considered to produce reliable results, especially when the goal is to test gene-gene interactions (for a discussion of methodological issues around the use of genetic data in neuroscience see Green et al., 2008). Therefore, all these intriguing results should be considered preliminary and interpreted with caution. Future genome-wide association studies and full genome sequencing would provide valuable information about the genetic aspects of creativity.

2. The dopaminergic systems from a clinical neuroscience perspective

Considering the broad range of functions DA supports, it is not surprising that several neuropsychiatric disorders are characterised by abnormalities in DA function. We are going to discuss three disorders that are known to be associated with disturbances in the DA system, namely schizophrenia, ADHD, and Parkinson's disease (PD). Moreover, we go beyond the borders of the clinically diagnosed disorders, and consider the extended phenotypes related to these disorders.

The conjecture that mental disorders are extremes of normal personality variation has a long history both in psychiatry and differential psychology. Several influential theorists of individual differences have suggested models of personality to account for normal and pathological functioning at the same time (Cloninger, Svrakic, & Przybeck, 1993; Eysenck, 1993). This tradition is paralleled by the endophenotype concept in psychiatric research. The aim of the endophenotype approach is to find state-independent, heritable phenotypes that are not only associated with a given psychiatric illness, but are also prevalent in unaffected relatives of people with the illness (Gottesman & Gould, 2003). Importantly, thinking about mental disorders in terms of dimensionality has recently been infiltrating into psychiatric classification systems. After lengthy debates among experts, the dimensional perspective on personality disorders have made its way to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders, although the previously established categories of personality disorders have remained in the manual (Krueger & Markon, 2014). The notion of continuity between mental

disorders and normality is not only appealing from a moral viewpoint (David, 2010), but there is also data in its support. Validity and reliability of dimensional representation of mental disorders have gained support from a meta-analysis, which argued that using discrete disorder categories instead of dimensions leads to loss of important information (Markon, Chmielewski, & Miller, 2011). So while diagnostic categories may support efficient decision making in medicine and facilitate epidemiological research, this does not imply that the underlying latent constructs representing mental disorders are strictly categorical. However, it is important to note that at least three continua can be considered (Linscott & van Os, 2010): the continuum of experience (e.g. Do healthy people have experiences that are similar to signs and symptoms of mental disorders?), the continuum of population structure (e.g. Can we statistically separate healthy, subclinical, and mentally disordered subpopulations?), and the continua between mental disorders (e.g. Are schizophrenia and bipolar disorder discrete entities?).

2.1 Schizophrenia

2.1.1 The psychosis continuum

The observation that psychotic-like experiences are reported by around 5% of the general population led to the notion of the **psychosis continuum** (see the review by van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2008). Importantly, the prevalence of psychotic-like experiences is related to demographic (e.g. unemployment and migration) and aetiological factors (e.g. cannabis use, trauma, and urbanicity) that are associated with increased risk of schizophrenia. In most cases, psychotic-like experiences are transient and do not evolve into a psychotic disorder. On the other hand, when psychotic-like experiences persist and co-occur with aetiological risk factors, a transition to a psychotic disorder is more likely to occur.

Schizotypy is a central concept of the psychosis continuum. It refers to a set of stable personality traits that resemble the signs and symptoms of schizophrenia in a subclinical manner (Ettinger, Meyhofer, Steffens, Wagner, & Koutsouleris, 2014). There is agreement in the literature in that schizotypy is **multidimensional**, with aspects corresponding to symptom domains of schizophrenia. The exact number and content of the dimensions, however, remains to be debated, and it seems that variation in samples and instruments could explain some of the heterogeneity in the findings. Vollema and Bosch (1995) presented a review of various self-report scales designed to measure schizotypy. According to their summary, factor-analytic studies implicated that schizotypy consisted of three or probably four factors. They highlighted the consistency of positive, negative, and nonconformity dimensions, while a factor representing social anxiety and cognitive disorganisation was not supported by replication

studies at that time. Finally, the positive and the negative dimensions of schizotypy had further support from clinical validation studies. For example, a study where non-psychotic psychiatric inpatients filled the Schizotypal Personality Questionnaire (SPQ) reported that three factors provided the best fit to the data, which were termed positive, negative, and disorganised schizotypy (Vollema & Hoijtink, 2000). Another study found that a similar three-factor model (cognitive-perceptual, interpersonal deficits, and disorganisation) provided best fit to SPQ data obtained in patients with schizophrenia and in university students as well (Rossi & Daneluzzo, 2002). On the other hand, a study where more than six thousand university students filled the Wisconsin Schizotypy Scales, which contained items related to hallucination- and delusion-like experiences, and physical and social anhedonia, unsurprisingly obtained a positive and a negative schizotypy dimension (Kwapil, Barrantes-Vidal, & Silvia, 2008). Finally, several authors have argued in favour of a four-dimensional model of schizotypy, comprising a positive, a negative, a disorganised, and an impulsive nonconformity dimension. The latter dimension is analogous to Eysenck's concept of psychoticism (Eysenck, 1993), and it is measured with items tapping affective dysregulation and impulsive, aggressive, and asocial behaviour. The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE) is a widespread instrument associated with the four-dimensional model of schizotypy (Claridge et al., 1996; Fonseca-Pedrero, Ortuño-Sierra, Mason, & Muñiz, 2015; Mason, Claridge, & Jackson, 1995). The four-factor structure of schizotypy, however, has been questioned by a study which examined 228 help-seekers, who had previously been identified as ultra-high risk for psychosis (A. Lin et al., 2013). In this highly schizotypal sample, the impulsive nonconformity dimension of schizotypy appeared unstable in factor analyses. The three-factor model was shown to be robust, which consisted of a positive, a negative/interpersonal, and a disorganised dimension.

Recently, the evidence from behavioural, psychopharmacological, and neuroimaging studies has been reviewed in two articles written by two independent groups of researchers. Globally, these articles argued for a **continuum** and overlap between schizotypal traits in healthy people and schizophrenia symptoms **at multiple levels** of analysis (Ettinger et al., 2014; M. T. Nelson, Seal, Pantelis, & Phillips, 2013). For example, schizotypy is associated with subtle impairments in the domains of attention, working memory, executive functions, and motor control. As patients with schizophrenia are frequently reported to have a remarkable deficit on these measurements, the authors of these reviews argued that schizotypy in the general population and schizophrenia represent different ranges of the same continuum. However, the picture is less clear for structural and functional neuroimaging findings. For

instance, a structural magnetic resonance imaging study examining participants with high positive schizotypy have found less grey matter volume in cortical (e.g. medial prefrontal and temporal areas), but not subcortical regions involved in schizophrenia (Ettinger et al., 2012).

2.1.2 Criticisms of the continuum view and possible resolutions

Several authors have raised concerns about considering the continuum between schizotypy and schizophrenia simply linear. First, it should be pointed out that how psychotic-like phenomena are measured (interview vs. questionnaire, leading questions in surveys, like 'psychotic experiences are quite common', etc.) matters a lot with respect to their observed distribution in the population. Second, there are some **key qualitative differences** between sub-clinical and clinical psychotic phenomena. For example, according to David (2010), research has shown that the contents of subclinical and clinical delusions are similar, whereas the degree of the associated distress, conviction in the belief, and preoccupation can distinguish clinical delusions from odd subclinical beliefs. Distress, conviction, and preoccupation go together for most delusional beliefs, in that delusions that are held with greater conviction are more likely to cause distress and preoccupation. However, it has been suggested that conviction might not predict distress and preoccupation in case of religious and spiritual beliefs. To sum up, David concluded that 'psychopathological phenomena are continuous but risk for schizophrenia is not' (2010, p. 1940).

Kaymaz and van Os (2010) suggested a distinction between the continuum and the extended phenotype. They additionally pointed out that syndrome clusters described in patient populations could be extended to the healthy population. The authors speculated that people reporting subclinical psychotic experiences could represent two latent groups. Members of one group might have psychotic experiences without motivational and cognitive deficits, who will be unlikely to develop psychotic disorders. Another group might involve people experiencing psychotic phenomena, and suffering from cognitive and motivational problems; they are expected to be at significant risk of transitioning into frank psychosis.

In their comprehensive review, Linscott and van Os (2010) discussed important aspects of the continuous-categorical debate. They pointed out that **continuity can have several meanings** as used in the context of schizophrenia research. First, one may investigate whether the processes behind schizophrenia are the same that are behind schizotypy and psychotic-like experiences in the general population. Second, intraindividual continuity of experiences during the course of schizophrenia can be considered. Third, the questions about continuity in population structure are concerned with whether the observed variation in schizophrenia and

schizophrenia-like phenotypes is a result of smooth differences between the members of a single population, of the mixture of multiple latent discrete populations, or of a combination of these scenarios.

With respect to the phenomenological continuity issue, Linscott and van Os (2010) pooled results of studies investigating the prevalence rates of schizophrenia-like experiences in the general population. They have concluded that there seems to be a continuum at the level of experience, in that psychotic-like experiences are relatively common in the general population, as compared to prevalence rates of schizophrenia. Additionally, they found remarkable variance in the rate of hallucinations, delusions, disorganised speech, negative symptoms, and social isolation reported in studies examining samples from the general population. Some of this variation was explained by demographical and environmental factors known to increase the risk for developing schizophrenia, such as unemployment, lower income, less education, minority status, or using cannabis and other drugs, just to name a few. Strikingly, over half of the variance in the reported prevalence rates was explained by methodological variables like characteristics of the sample (e.g. convenience sampling, sample size), assessment mode (e.g. self-report vs. interview, number of items), criterion variables (e.g. exclusion or response criteria), and analytical decisions.

In relation to the debate about the **continuous versus categorical** nature of population structure, an additional qualitative review was carried out on studies examining the distribution of schizophrenia-like phenotypes (Linscott & van Os, 2010). It should be emphasised that factor analysis, cluster analysis, or latent class analysis are not designed to answer questions of dimensionality; therefore, the authors only considered studies which used factor mixture modelling or coherent-cut kinetic, which can provide direct statistical evidence for latent continua or categories. They have found that out of such analyses reported in the literature, around two-thirds have found evidence in favour of a non-arbitrary boundary between normality and schizophrenia, while the rest have reported evidence supporting a latent dimensional structure. To sum up, there appears to be a continuity of psychotic experiences in the population, while the underlying population structure seems rather categorical, although the evidence is far from conclusive. In addition, overcoming the excess reliance on self-report and interview techniques would help the field moving forward.

2.1.3 The dopamine hypothesis of schizophrenia and its extension to related phenotypes

Dopamine abnormalities have been among the dominant explanation of schizophrenia since the discovery of antipsychotics in the middle of the 20th century. The initial view that

schizophrenia is caused by elevated DA levels has been updated in the early nineties, when striatal hyperdopaminergia was suggested to be responsible for positive symptoms, while prefrontal hypodopaminergia was supposed to underlie negative symptoms and cognitive impairment (Davis, Kahn, Ko, & Davidson, 1991). The **dopamine hypothesis of schizophrenia** has been refined by Howes and Kapur (2009), who made several important claims. Their theory concentrated on providing a comprehensive and specific explanation of psychosis. Beyond several other striatal dopaminergic abnormalities, elevated striatal presynaptic DA synthesis capacity was suggested to be the key neurochemical mechanism behind psychosis. According to Howes and Kapur (2009), the interaction of multiple causes such as genetic factors and various environmental effects (reviewed in Brown, 2011; Réthelyi, Benkovits, & Bitter, 2013; van Os et al., 2008) contribute to striatal DA dysregulation. In turn, disorganised striatal DA signalling leads to aberrant attribution of salience, setting the stage for psychosis. Importantly, Howes and Kapur (2009) suggested that the dopamine hypothesis can be extended beyond schizophrenia, in that it can explain psychosis in other mental disorders and also psychotic-like phenomena in psychosis prone individuals.

Addressing the latter issue, Mohr and Ettinger (2014) presented a comprehensive summary of the literature addressing whether dopaminergic neurotransmission is altered in healthy people scoring high on self-report schizotypy questionnaires. They overviewed psychopharmacological studies investigating basic behavioural markers, higher cognitive functions, and also molecular genetic and imaging research. According to this review, some of the variation in schizotypy observed in the healthy population can be explained by alterations in the DA systems, although the molecular genetic and imaging literature is relatively scarce. Moreover, some of the cognitive deficits associated with high schizotypy seem to improve following the administration of DA agonists and antagonists as well. Importantly, such compounds were often shown to have opposing effects on cognition in low schizotypy.

Finally, the observation that psychosis and psychotic-like experiences can emerge in PD during dopaminergic therapy is in line with the dopamine hypothesis of schizophrenia (Howes & Kapur, 2009). A detailed discussion of psychosis and psychotic-like experiences in PD will be provided in a later chapter.

2.1.4 Psychosis and creativity

The notion that creativity is associated with vulnerability to mental disorders, including psychosis, goes back to antiquity (Thys, Sabbe, & De Hert, 2013). In his seminal paper, Eysenck (1993) has outlined several ideas that were later proven highly influential on how

creativity's association with madness was approached by scholars. Eysenck emphasised that **psychosis proneness** (psychoticism in his terminology) **is beneficial to** trait **creativity** (e.g. originality measured by tests of divergent thinking) and creative achievements (e.g. real world creativity and eminence), while psychotic disorders prevent individuals from fulfilling their creative potentials. The main conclusion was that high psychoticism is more likely to promote creativity in the presence of protective factors like ego-strength and personal efficiency. Several cognitive features that link psychosis proneness and creativity were identified, such as overinclusive thinking, unusual word associations, reduced latent inhibition, and lack of negative priming (reviewed in Eysenck, 1993). At that time, when neuroscience data on the correlates of creativity were scarce, several hypotheses were made with regard commonalities between madness and creativity at the neurobiological level (Eysenck, 1993). In particular, individual differences in the hippocampal formation, and in dopaminergic and serotonergic neurotransmission were identified as potential links between creativity and psychosis proneness. As we have seen, some of these speculations have gained empirical support since then (see 1.2.3 and 2.3.1).

Psychosis proneness, as indicated by familial risk, have been found to be associated with creative occupations. Studies examining the familial association between mental disorders and creativity have reported that parents and siblings of patients with schizophrenia and schizoaffective disorder are more likely to have a creative profession than those who do not have a first degree relative with a psychiatric disorder (Kyaga et al., 2011, 2013). In addition, one of these studies has shown that people with schizophrenia or schizoaffective disorder are less likely to have a creative occupation, relative to healthy controls (Kyaga et al., 2013). On the other hand, diagnosis of bipolar disorder was associated with increased likelihood of having a profession that demands creativity (Kyaga et al., 2011, 2013). Furthermore, meta-analyses that examined trait-level indicators of psychosis proneness have revealed associations with creativity of small effect size. A meta-analysis based on 45 studies has found that schizotypy dimensions were slightly associated with various indicators of creativity. Specifically, positive and impulsive schizotypy were positively (r = 0.14), while negative and disorganised schizotypy were negatively associated with creativity (r = - 0.09) (Acar & Sen, 2013). A qualitative review concluded that psychoticism was strongly related to artistic creativity, less strongly to creativity in science, and moderately to everyday creativity (i.e. creative activities and divergent thinking) (Batey & Furnham, 2006). Another meta-analysis that covered 32 studies examining the link between psychoticism and creativity has found a similarly small (r = 0.16), but more heterogeneous relationship, indicating that psychoticism had a small

correlation with creativity. A follow up analysis revealed that the effects were significantly larger (r = 0.50) if uniqueness of divergent thinking was taken as the indicator of creativity and psychoticism was measured by the Eysenck Personality Questionnaire (Acar & Runco, 2012).

In our review of the literature we have argued that the link between schizotypy and creativity can be explained by similarities at the level of basic cognitive processes such as latent inhibition, pattern perception, and remote semantic associations (Thesis point 1, Polner & Kéri, 2015). We have extended previous theoretical work in this field (Eysenck, 1993) in multiple ways. First, we have reviewed evidence that supported the role of DA in the overlap between schizotypy and creativity. Second, we have described similarities and differences between schizotypy and openness at the phenomenological, the cognitive, and the neural level, building on research and theory from differential psychology (DeYoung, 2013; DeYoung, Grazioplene, & Peterson, 2012)

Creativity has not only been linked to proneness towards psychotic disorders, but its association with subtle or full-blown forms of various other psychopathologies has been suggested as well. Of particular relevance to the present discussion, ADHD has been suggested to support creativity in some manner, and DA treatment in Parkinson's disease have been reported to reveal hidden creative potentials. We are going to discuss these issues in the chapters corresponding to these disorders.

2.2 Attention-deficit/hyperactivity disorder

Attention-deficit/hyperactivity disorder (ADHD) is characterised by symptoms of inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2000). Although diagnostic systems imply strictly defined categories, research has shown that children and adults can be classified into several subgroups along ADHD-related symptomatology, demonstrating substantial heterogeneity within the disorder (e.g. Fair, Bathula, Nikolas, & Nigg, 2012; Kóbor, Takács, Urbán, & Csépe, 2012).

2.2.1 The ADHD continuum and neurocognitive impairment

Beyond heterogeneity of the clinical disorder, the diagnostic boundaries of ADHD are somewhat arbitrary in an additional sense as there appears to be a **dimensional continuum of ADHD**. On the lower end of this continuum we find healthy people who do not show ADHD-like traits at all, healthy people with a high level of ADHD-like traits lie in the middle, while the upper end is occupied by individuals with a clinical diagnosis of ADHD. Such dimensional representation of ADHD has gained support from several studies.

A twin study has reported similar heritability estimates of ADHD phenotypes no matter whether they were considered categorical (diagnosis) or dimensional (number of symptoms) (Levy, Hay, McStephen, Wood, & Waldman, 1997). The authors concluded that in light of these results the dimensional account should be favoured over the categorical one, as the relationship between heritability and ADHD-like phenotype was not moderated by diagnostic categories. A later study applied taxometric analyses to a wide range of indicators (parent and teacher rated ADHD-like behaviours, sustained attention, executive control processes, and intelligence) obtained in a large sample of children drawn from general population (Marcus & Barry, 2011). Taxometric analyses can be used to statistically determine whether the underlying population structure is more likely to be dimensional or categorical. Importantly, the results suggested that both ADHD-like traits in general and the dimensions of inattention and hyperactivity/impulsivity were dimensional as well. These findings were later confirmed in a sample of adults, some of whom were healthy while others were diagnosed with Axis I/II psychopathologies (Marcus, Norris, & Coccaro, 2012), suggesting that the latent continuum crosses diagnostic borders. Dimensional representation of ADHD might be of clinical utility, as a study has shown that symptom counts of inattention and hyperactivity/impulsivity could predict subsequent functional impairment in children (Lahey & Willcutt, 2010).

An early influential theory suggested that **inhibitory impairment** is central to ADHD symptoms (Barkley, 1997). Indeed, patients with ADHD have been shown to have impairment on various tasks measuring inhibition-related functions (i.e. response inhibition and interference control, following N. P. Friedman & Miyake, 2004). According to a meta-analysis covering a substantial amount of research (number of studies ranged from 69 to 94), ADHD is characterised by a moderate deficit of response inhibition (Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014). It should be noted, however, that such a deficit was not specific of ADHD as it was present in various other mental disorders (such as obsessive-compulsive disorder, depression, or schizophrenia, to name a few). What is more, several other impairments are present in ADHD, such as deficient temporal processing, increased delay aversion, reduced visuo-spatial working memory (Castellanos & Tannock, 2002), or increased intra-individual variability, mirrored by fluctuating performance (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006). Importantly, the dimensional model of ADHD has gained additional empirical support at the neurocognitive level. For instance, unaffected siblings of children with ADHD demonstrated an intermediate-level deficit of inhibition-related functions (Slaats-Willemse, Swaab-Barneveld, De Sonneville, Van Der Meulen, & Buitelaar, 2003). Moreover, in a sample of 16 099 children and adolescents drawn from the general population

(6% had a clinical diagnosis of ADHD), response inhibition, response latency, and variability were mildly associated with a trait marker of ADHD (Crosbie et al., 2013). However, it should be noted that these participants were not tested in experimental laboratories but at a science centre, which might have confounded the findings.

In our study, we examined the relationship between ADHD-like traits and laboratory tests of inhibition-related functions in a large sample of healthy adults (Thesis point 2, Polner, Aichert, Macare, Costa, & Ettinger, 2015). On two out of the six tasks applied, we found subtle associations between inhibition-related functions and ADHD-like traits. Put more precisely, performance on the go/no-go and the Stroop tasks predicted self-report indicators of ADHD-like traits. Importantly, neuroticism robustly and positively predicted ADHD-like traits, indicating that difficulties in negative affect regulation are associated with inattentive and hyperactive/impulsive tendencies in the general population.

Inspired by neurobiological and computational studies, it has been suggested that prefrontally mediated deficits of response inhibition might not primarily reflect problems in inhibition per se, but can stem from the impaired representation of goal and context in PFC (Munakata et al., 2011). According to this view, one may argue that response inhibition deficits associated with ADHD-like traits might be due to the insufficient maintenance of the most adaptive task sets in the PFC, thus providing a link between the neurocognitive impairment on the ADHD spectrum and exploration. In the following section, we will argue that the molecular genetic and computational literature on ADHD is in line with conceptualising ADHD as an exploratory phenotype.

2.2.3 Dopamine involvement in ADHD

Dopamine involvement in ADHD is implicated by molecular genetic studies that have revealed that certain variations in DA genes can increase the risk for child and adult ADHD. In addition, some DA gene variants were found to predict differences in ADHD-like traits in healthy adults.

In a review by Faraone and colleagues (2005), the picture emerging from candidate gene studies of ADHD appeared coherent: several genes related to the dopaminergic systems were associated with ADHD. For example, DA receptor genes (DRD4 and DRD5), the DA transporter gene (DAT), and the dopamine beta-hydroxylase (DBH, dopamine to norepinephrine conversion) all appeared to increase risk for ADHD across adult and child samples. It should be noted that when the authors analysed the available studies together, the

pooled effect sizes were modest, suggesting that ADHD-risk is modulated by multiple genes of small effect.

A more recent review on the genetics of adult ADHD have concluded that genes related to the dopaminergic systems, such as the DAT, or the DRD4 and the DRD5 genes, are associated with ADHD persisting into adulthood (Franke et al., 2012). It should be noted, however, that in some studies, the alleles associated with risk for adult ADHD differed from the alleles that previously had been found to increase risk for ADHD in childhood. Although the comparison of these reviews suggests that the genetic components of childhood and adult ADHD partly differ, from our point of view, the relevance of dopaminergic genes for both forms of the disorder is particularly noteworthy.

An explorative study investigated the genetic influences on ADHD-like traits in the general population (Reuter, Kirsch, & Hennig, 2005). According to the results, polymorphisms of genes related to the dopaminergic (COMT enyzme) and serotonergic (5-HT2a receptor) systems were associated with hyperactive and inattentive traits in 203 healthy participants. Participants lacking the Val allele of the COMT gene displayed greater inattention and hyperactivity/impulsivity, relative to Val carriers. Participants without the C allele of the 5-HT2a gene had greater hyperactivity/impulsivity, relative to those who carried the C allele of the gene. Although the authors claimed that the study spoke for the external validity of ADHD-like traits in the general population, it should be underlined that the polymorphisms identified by Reuter et al. (2005) were not conclusively shown to confer risk for ADHD (for reviews see Faraone et al., 2005; Franke et al., 2012). A more recent study has shown that DAT polymorphisms were associated with higher self-reported ADHD-like traits in 517 healthy adults (Tong et al., 2015). It should be noted, however, that the haplotype copy of the DAT gene that yielded an effect in this study had been linked to childhood (Faraone et al., 2005), rather than adult ADHD (Franke et al., 2012).

Individual variation in DA genes seems to be related to the phenotypic expression of ADHD and the related attentional and neural deficits. For instance, a study has found that the risk allele of the DAT1 gene was associated with greater deficit of spatial inattention in child ADHD, and this variant of the DAT1 gene was also associated with a gentle attentional deficit among healthy control children (Bellgrove et al., 2009). Additionally, striatal response to reward in a rewarded task-switching paradigm was aberrantly high in adults with ADHD who carried the 9-repeat variant of the DAT gene (Aarts et al., 2015). The neural response to reward in the striatum was normalised by methylphenidate (a drug used to treat ADHD which

modulates DA neurotransmission) in these participants. No such alteration of neural response was observed in adults with ADHD who carried the 10-repeat variant of the gene.

Novel insight into the role of DA in ADHD has been provided by the recent computational framework of Hauser, Fiore, Moutoussis, and Dolan (2016). These authors have proposed that behavioural phenotypes related to ADHD could be caused by impaired modulation of neural gain in cortico-striatal loops. Dopaminergic and noradrenergic neurotransmission are assumed to have a key role in such modulation. Computationally, neural gain indicates the extent to which neural signals are amplified or attenuated. Neural representations are stable in high neural gain states and are unstable in low neural gain states. The latter bias the system towards exploration, and indeed, ADHD behaviours can be conceptualised as extremely explorative choice behaviour. A high decision temperature, which indicates greater stochasticity in choices, is associated with smaller likelihood of choosing the action believed to be the best. Importantly, the performance of patients with ADHD on a continuous performance task suggested that high decision temperature might explain the behavioural inconsistencies observed in multiple domains.

2.2.4 ADHD and creativity

Several studies have investigated the association of ADHD and creativity, a prominent behavioural indicator of exploration (DeYoung, 2013). A recent meta-analysis has examined how ADHD is related to various forms of little-c creativity (Kaufman & Beghetto, 2009), that is, performance indicators of divergent thinking, drawing, problem solving, and self-reported creative personality traits (e.g. being imaginative or curious), and engagement in creative activities (Paek, Abdulla, & Cramond, 2016). This meta-analysis yielded a significant, small and negative mean effect size (r = - 0.17) for the association between ADHD and creativity. When studies that examined creativity in relation to anxiety- and depression-related psychopathology were pooled together with studies on ADHD and creativity, significant moderators of the association emerged: the type of psychopathology assessment (negative association for clinical methods but positive for self-report) and the type of creativity assessment (negative association for performance indicators but positive for self-report). Sadly though, it has not been clarified whether these variables moderated the specific association of ADHD with creativity. Nevertheless, besides revealing a small and negative correlation between ADHD and creativity, this meta-analysis study drew attention to the heterogeneity of the relationship, suggesting that ADHD might boost and impair certain aspects of creativity at

the same time. In order to understand this controversial association, we are going to have a closer look at some illustrative studies.

Shaw (1992) measured a set of variables putatively related both to ADHD and creativity in control and attention-disordered and hyperactive (ADH) children, who did not have a clinical diagnosis of ADHD. The latter group of children was characterised by reduced right laterality, enhanced unconscious perception of relationships, crossed eye-hand dominance, spending less time with unsolved anagrams, superior figural divergent thinking, higher sensation seeking, better incidental learning of object – context relationships, imaginative problem solving style, and increased utilisation of information presented in the periphery when solving anagrams. Curiously, tacit perception of relationships (as indicated by rapidly detecting an associative relationship between a target stimulus and surrounding stimuli while focussing on the target) was the only variable that predicted both figural creativity and discriminated ADH children from controls. Thus one may argue that leaky attentional processing style is the common basis of ADH phenotypes and divergent thinking ability.

Another study has measured semantic inhibition, plus divergent and convergent thinking in adults with ADHD and controls (White & Shah, 2006). The adults with ADHD examined here can be considered high functioning, as they were not inferior to the controls in terms of academic achievement. As opposed to divergent thinking, convergent thinking is used to solve problems which have one exact correct solution. In this study, it was measured with the remote association task, where participants are shown word triads and have to come up with a fourth word that is related to all of the words shown (Mednick, 1962). Adults with ADHD outperformed the controls on all indicators of verbal divergent thinking (originality, fluency, and flexibility), while they had impaired convergent thinking and semantic inhibition. Follow-up analyses showed that deficit of semantic inhibition mediated the association of ADHD with convergent, but not divergent thinking. Individuals with ADHD might be at advantage at the ideation phase of the creative process, when divergent thinking is required, but their problems with inhibiting semantically unrelated information might hinder them when it comes to evaluating and implementing their ideas (see Amabile, 1983). These findings were replicated and extended by a later study (White & Shah, 2011). University students with ADHD produced more original ideas on a verbal task of divergent thinking, and also reported more real life creative achievement in art and science. Interestingly, when compared to the ADHD group, controls preferred to define and structure problems, and to elaborate and refine ideas. On the other hand, adults with ADHD reported a greater preference to generate ideas.

A study of children with ADHD yielded paralleling results (Abraham, Windmann, Siefen, Daum, & Güntürkün, 2006). Relative to controls, children with ADHD were less constrained by exemplar toys when asked to design a novel toy. On the other hand, when required to imagine a functional object composed of pre-defined geometric objects, tools designed by children with ADHD were rated less practical, than those designed by the control children. No significant differences were found between ADHD and control children in terms of the originality of these tool designs, or in fluency or uniqueness of verbal divergent thinking. Regarding null findings, we note that another paper that compared children with and without a diagnosis ADHD also reported no significant differences between the groups in terms of various indicators of figural divergent thinking (except for elaboration, which was higher among control children) (Healey & Rucklidge, 2005).

A later study has tested gifted children with and without ADHD-like traits (without a clinical diagnosis of ADHD) (Fugate et al., 2013). The criteria of giftedness were an IQ of 120 or above and outstanding academic achievement. The groups were matched in terms of fluid intelligence and academic achievement. On measures of working memory, control children outperformed children with ADHD, while the latter group had superior performance on a task that measured figural divergent thinking. The latter effect was driven by more elaborated drawings and abstracter titles in the ADHD group. Enhanced divergent thinking in the ADHD group is especially noteworthy given that in the sample, working memory correlated negatively with divergent thinking, and the ADHD group had an impairment in working memory of a medium effect size, relative to the controls. It can be argued that when asked to come up with novel and useful ideas, gifted children with ADHD might adopt compensatory strategies that rely on cognitive resources other than working memory.

To sum up, the global picture suggests that ADHD-like traits can be beneficial in the ideational phase of the creative process, when divergent thinking is assumed to have primary importance (White & Shah, 2011). Furthermore, we argue that ADHD-like traits are associated with creative potential and achievement when they co-occur with high intelligence and normal academic achievement (Fugate et al., 2013; White & Shah, 2011) and probably when their severity does not lead to a clinical diagnosis (Fugate et al., 2013; Shaw, 1992), similarly to what has been argued about the link between psychosis and creativity (see 2.1.4). Placing the picture in a broader perspective, an evolutionary-oriented simulation study provided novel clues to understand how ADHD-like phenotypes could help groups to discover and utilise hidden resources (Williams & Taylor, 2006). The authors argued that behavioural variability or unpredictability, a key characteristic of ADHD (Hauser et al., 2016), leads to exploration and

the improvement of knowledge. Williams and Taylor (2006) modelled groups foraging food in a changing environment, and simulated hyperactive-impulsive ADHD with unpredictably behaving agents. Groups, where 5% of the members were unpredictable, performed the best: they could gain knowledge about food quality, and they also choose which food to eat according to this information. This resulted in greater survival rate, relative to groups composed of purely predictable or unpredictable agents. The former groups did not discover the more valuable sources of food, while the latter groups did, but failed to use this information to guide their future choices. The authors concluded that by definition, exploration is risky. Therefore when a minority of a group carries out risky exploration, and shares the acquired knowledge with the others, the whole group can enjoy the benefits of exploration. In the following section, we will see how explorative and impulsive tendencies can be induced by dopaminergic treatment in patients with Parkinson's disease.

2.3 Parkinson's disease

Parkinson's disease (PD) is a neurodegenerative disease with diverse symptoms. According to a neuroanatomically based staging scheme, the striking motor symptoms such as tremor, rigidity and bradykinesia emerge at intermediate stages when neurodegenerative processes reach dopaminergic neurons of the substantia nigra (SN), leading to depletion of striatal DA (Hawkes, Del Tredici, & Braak, 2010). We note here that PD has various other motor and non-motor symptoms, and neurotransmitter dysfunction in PD is not restricted to DA (for details see Brichta, Greengard, & Flajolet, 2013; and Hawkes et al., 2010).

2.3.1 Side effects of dopamine treatment in PD and the overdose hypothesis

The mainstream pharmacological treatment of motor symptoms of PD relies on levodopa and DA agonists (Akbar & Friedman, 2015). Dopaminergic treatment can have various side effects, including, but not limited to **impulse control disorders** (ICDs, pathological gambling, compulsive sexual, buying and eating behaviour), dopamine dysregulation syndrome (addiction-like state comprising excessive self-medication with DA drugs), and some further impulsive-compulsive behaviours (punding, hobbyism, walkabout, and hoarding) (Weintraub & Nirenberg, 2013). A study involving more than three thousand patients with PD found at least one active ICD in 14% of patients, of whom 29% percent experienced two or more ICDs. Pathological gambling was detected in 5%, compulsive sexual behaviour in 3.5%, compulsive buying in 5.7%, and binge eating in 4.3% percent of the patients (Weintraub et al., 2010). In addition, and importantly for the present discussion, medicated patients with PD might experience **psychotic symptoms and** develop **psychosis**. According to

an overview, prevalence rates of complex visual hallucinations are relatively more heterogeneous (22-38%) than that of auditory hallucinations (0-22%) or minor psychotic symptoms (17-72%) (Fénelon & Alves, 2010), while the lifetime prevalence of visual hallucinations in PD was around 50% in a study (D. R. Williams & Lees, 2005). Finally, delusions seem to affect circa 5% of patients with PD (Fénelon & Alves, 2010). Hallucinations in PD have been suggested to arise from the complex interplay of dopaminergic dysregulation and cholinergic imbalance, disease-specific alterations at the level of the brain and the retina, altered regulation of sleep-wake cycles, and impairment of visual attention (Diederich, Fénelon, Stebbins, & Goetz, 2009).

Interestingly, immersion in **creative activities and** elevated **creative achievements** have been reported to co-occur with dopaminergic therapy in PD. Increased creativity has been described in various domains of art, such as in poetry and writing (Canesi, Rusconi, Isaias, & Pezzoli, 2012; Joutsa, Martikainen, & Kaasinen, 2012; Schrag & Trimble, 2001), visual arts (Canesi et al., 2012; Chatterjee, Hamilton, & Amorapanth, 2006; Kulisevsky, Pagonabarraga, & Martinez-Corral, 2009; López-Pousa et al., 2012; Walker, 2016; Walker, Warwick, & Cercy, 2006), and sculpture (Canesi et al., 2012). Some of the above studies pointed out the phenomenological similarities between ICDs and creativity in PD, highlighting the compulsive nature of artistic activities pursued by some patients (Joutsa et al., 2012; Kulisevsky et al., 2009). According to a survey involving 290 patients with PD, ICDs were significantly more common in patients with PD who reported increased creativity, relative to those who did not (Joutsa et al., 2012). On the other hand, two studies reported no significant association between ICD and creativity in PD, although these studies might have been statistically underpowered to detect an effect (Canesi et al., 2012; Faust-Socher, Kenett, Cohen, Hassin-Baer, & Inzelberg, 2014). Another case study reported that initiation of DA replacement therapy revealed hidden poetic talent of a patient, who was very productively writing poems in the first year of DA therapy, could publish his work, and even won an award. Approximately a decade after, the patient started to suffer from affective problems (depression and aggression), then later developed paranoid and manic symptoms (Schrag & Trimble, 2001), suggesting that propensity to the facilitative effect of DA drugs on creativity in PD might overlap with proneness towards psychosis and affective dysregulation.

A few studies have systematically examined creative thinking skills of patients with PD receiving DA replacement therapy. The Canesi et al. (2012) study examined verbal and visual divergent thinking in patients with PD who had started to engage in artistic creativity after the onset of DA therapy, and in patients who did not. Relative to the controls, the latter group of

patients with PD had impaired divergent thinking, due to reduced elaboration scores. Divergent thinking scores of creative PD patients did not differ significantly from those obtained in the control group, suggesting that real life creative activities and achievements in PD are associated with preserved creative potentials. Another study suggested that divergent thinking in medicated PD patients can be a function of symptom onset. Patients with left hemibody symptom onset performed similarly to controls on a complex assessment of divergent thinking, while patients whose symptoms began on the right hemibody had fewer ideas on a verbal divergent thinking task (Drago, Foster, Skidmore, & Heilman, 2009). Importantly, the patient groups did not differ significantly from controls in terms of general verbal fluency, suggesting that the differences are unlikely to stem from a broader executive impairment. Finally, a study assessed a range of cognitive abilities associated with creativity, namely insight problem solving, verbal and visual divergent thinking, and understanding of novel metaphors (Faust-Socher et al., 2014). According to the results, patients with PD outperformed controls in terms of fluency and quality of divergent thinking in the verbal domain, and were also superior in understanding novel metaphors.

Last but not least, DA replacement therapy in PD can have contrasting **effects on** various **cognitive functions**. Cools (2006) has argued that the controversies in the literature on cognition in PD and DA treatment can be explained by a) different task demands such as cognitive stability vs. plasticity, and by b) different DA levels in the structures supporting performance on the tasks.

First, cognitive stability (related to maintenance) is related to D1 receptor activation in the PFC, while cognitive flexibility (related to task switching) is related to D2 receptor activation in striatum. After critically evaluating the literature, Cools (2006) concluded that flexible switching between well-established task-sets is impaired in patients with PD, and that this impairment can be reversed by levodopa. Moreover, Cools added that simple maintenance of information (as measured by simple tasks that do not tax flexibility at all) might be intact in PD and unaffected by levodopa.

Second, according to the **'over-dose' hypothesis** (first proposed by Gotham, Brown, & Marsden, 1988), the effect of DA therapy in PD on a given cognitive process depends on baseline DA levels in the structures underpinning that particular process. For example, in early stages of PD, DA levels are severely depleted in the dorsal striatum, while DA levels are relatively intact in the ventral striatum. Simply put, as the dose of DA therapy in PD is adjusted to ameliorate motor symptoms related the dorsal striatum, DA therapy optimises DA levels in dorsal striatum but might overdose DA in the relatively intact ventral striatum (see Figure 1).

Cools (2006) has proposed levodopa has different effect on distinct types of flexibility, which correspond to separable striatal subregions. That is to say, the dorsal striatum is implicated in switching between abstract rules or stimulus-response mappings, while the ventral striatum is involved in reversal learning and shifting between stimulus-outcome mappings. Levodopa withdrawal impairs task-switching, revealing the functional damage of the dorsal striatum in mild PD. Probabilistic reversal learning, supported by the ventral striatum, is improved by withdrawal, suggesting that DA levels in the ventral striatum are higher than optimal with levodopa (reviewed in Cools, 2006). It has to be noted here that the majority of the studies reviewed in the above article were conducted with patients on levodopa, although a few studies with DA agonist have suggested that similar effects could be expected with those compounds.

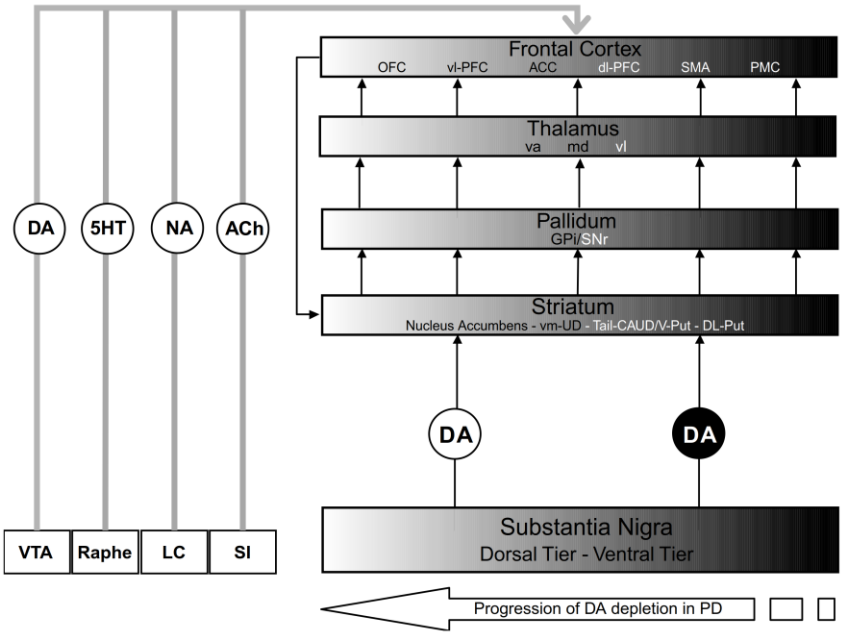

Figure 1. Schematic illustration of the selectivity of dopaminergic impairment during the progression of Parkinson's disease. Early on in the disease course, the dopamine neurons in the ventral tier of the midbrain are severely degenerated. These neurons project to the dorsal striatum, which is preferentially connected to the dorsal and lateral portions of the prefrontal cortex. On the other hand, dopamine neurons in the dorsal tier of the midbrain (including the VTA) remain relatively intact, therefore, dopaminergic functions in the loop consisting of the nucleus accumbens, and the ventrolateral and orbital portions of the frontal cortex are relatively spared.

Abbreviations: VTA, ventral tegmental area; DA, dopamine; Raphe, dorsal and medial raphe nuclei; 5-HT, serotonin; LC, locus coeruleus; NA, noradrenaline; SI, substantia innominata; ACh, acetylcholine; vm-CAUD, ventromedial caudate nucleus; Tail-CAUD, tail of the caudate nucleus; V-Put, ventral putamen; DL-Put, dorsolateral putamen; GPi, internal segment of the globus pallidus; SNr, substantia nigra pars reticulata; va, ventral anterior nucleus; md, dorsomedial nucleus; vl, ventrolateral nucleus; OFC, orbitofrontal cortex; vl-PFC, ventrolateral PFC; ACC, anterior cingulate cortex; dl-PFC, dorsolateral PFC; SMA, supplementary motor area; PMC, premotor cortex (adapted from Cools, 2006).

In the following section, we will selectively review studies on cognitive functions which are not only affected by PD and/or DA therapy, but are also potentially relevant to ICDs, psychosis and creativity in PD. Our study examining latent inhibition, anomaly categorisation, and schizotypy in PD will be referred to in this section. In the last section of the chapter, we will present a brief overview of the literature on individual differences in the effect of dopaminergic drugs on cognition in PD and health. This is motivated by the striking observation that so little is known about predictors of creativity after the introduction of DA drugs in PD. In this section, we refer to our longitudinal study which identified some pre-treatment traits which can predict the improvement of divergent thinking in PD after three months of dopaminergic therapy.

2.3.2 Reinforcement learning, salience, and latent inhibition

A classic finding concerning **reinforcement learning** in PD is that patients on dopaminergic medications (DA agonists and levodopa) show enhanced learning from positive feedback (reward), and are deficient in learning from negative feedback (punishment). This can be measured with probabilistic selection and deterministic transitive inference tasks, where participants' learning is driven by positive and negative feedback. Medication withdrawal has been found to reverse this pattern: patients who did not take their DA medications prior to the experiment demonstrated impaired learning from reward, but elevated learning from punishment (Frank, Seeberger, & O'Reilly, 2004). In a computational model, PD was simulated with reduced tonic and phasic DA activation a neural network, and DA medications with increased tonic and phasic DA activation (thus reducing the size of dips in DA activity associated with punishments). The computational model could successfully mimic how patients with PD performed in the experiment.

These results were replicated by a later study, where reinforcement learning was assessed in patients with PD before their first lifetime DA medications, and after twelve weeks of treatment with DA agonists (Bódi et al., 2009). Moreover, this study examined personality changes associated with DA treatment in PD. Reinforcement learning was measured with a probabilistic categorisation task where participants learned to categorise stimuli. For half of the stimuli, correct categorisation was rewarded with points, and no feedback was given for errors. For the other half of the stimuli, errors were punished with minus points, and no feedback was provided for correct categorisation. At the pre-treatment session, reward learning was impaired and punishment learning was elevated in the patients, relative to a matched healthy control group. In line with previous findings (Frank et al., 2004), DA agonists reversed this pattern: at

the follow-up, reward learning was similar to controls, and a remarkable deficit was observed in punishment learning. Medication had a significant influence on a personality trait associated with exploration (DeYoung, 2013): relative to controls, lower and higher novelty seeking was found in never-medicated and medicated patients with PD, respectively. Moreover, while novelty seeking and learning from reward showed a moderate positive correlation in healthy controls, this association was weaker and non-significant in never-medicated patients, but strong and positive in medicated patients. Thus it can be concluded that the DA agonist induced bias towards positive feedback leads to increased pursuing of novelty at the personality level.

A study used fMRI to measure reward prediction errors during reinforcement learning in a small sample of medicated patients with PD (Schonberg et al., 2010). This study measured reinforcement learning with computational estimates derived from performance on a slot machine task. In this task, participants had to choose one of two stimuli, which had different pre-defined probabilities of winning a reward (60 vs. 30 %). Choices of the patients and the controls did not differ significantly. The neural correlates of computationally estimated positive reward prediction errors (i.e. reflecting surprise caused by receiving a reward better than expected) revealed differential functional impairment in distinct striatal subregions: reward prediction error signalling was intact in the ventral, but not the dorsal striatum of the patients, while reward prediction errors were intact in both subregions of the control participants. The functional impairment restricted to the dorsal, but not the ventral striatum in PD is in line with the key premise of the overdose hypothesis (Cools, 2006).

To the best of our knowledge, two studies have examined adaptive and **aberrant salience** in patients with PD who were receiving dopaminergic therapy. Aberrant salience, that is, the attribution of meaning and significance to unimportant stimuli, is assumed to be the mechanism connecting striatal DA dysregulation to psychotic experiences (Howes & Kapur, 2009; Winton-Brown, Fusar-Poli, Ungless, & Howes, 2014). In both studies, salience attribution was measured with a speeded reaction time task that involved rewards. In this task, a cue that preceded target stimuli predicted the probability of reward on that trial. The colour and shape of the cues were varied; one of these dimensions indicated reward probability, while the other dimension was irrelevant. This task comprises implicit and explicit measures of adaptive and aberrant salience. Implicit salience is reflected by decreased reaction times associated with a given cue dimension, while explicit salience is measured with ratings of salience provided by participants; salience attributed to the valid and irrelevant cue dimensions are considered adaptive and aberrant, respectively.

One study examined salience attribution and schizotypy in PD patients with and without ICDs (Housden, O'Sullivan, Joyce, Lees, & Roiser, 2010). They have found reduced explicit adaptive salience in patients with PD who had no ICDs, relative controls and to patients with PD who had ICDs. Implicit adaptive salience was present in controls, but absent in both PD groups. This study did not find significant difference in aberrant salience. When the PD groups and the controls were collapsed together, explicit and implicit aberrant salience positively correlated with negative and disorganised schizotypy, respectively. Furthermore, standardised DA medication dose positively predicted impulsive schizotypy among the patients.

Another study assessed salience attribution and schizotypy in controls and never-medicated patients with PD before their DA agonist treatment was started. The participants were re-examined after a twelve week period, during which the patients continuously received DA agonist medications (Nagy et al., 2012). The tendency for psychotic-like experiences, as reflected by positive schizotypy, was increased by DA agonists. Relative to the controls, implicit and explicit adaptive salience was lower in patients with PD at the unmedicated baseline. DA agonists increased both adaptive and aberrant salience in the patients: that is, adaptive salience was normalised in the patients by the DA drugs, while aberrant salience was increased. In the medicated state, implicit and explicit measures of aberrant salience correlated with self-reported positive schizotypy. These results suggest that DA agonist induced aberrant salience might underlie psychotic-like experiences in PD, in line with theories emphasising the role of DA in aberrant salience associated with psychosis (Howes & Kapur, 2009; Winton-Brown et al., 2014).

A few studies have examined **latent inhibition** (LI, also see 1.2.2), or the related construct of negative priming in patients with PD. It can be argued that these paradigms are similar to aberrant salience to the extent that they measure the amount of processing capacity devoted to irrelevant stimuli. An early study examined LI in unmedicated patients with PD (Lubow, Dressler, & Kaplan, 1999). In this sample, LI appeared to be a function of laterality of symptom onset and gender: right-onset female patients demonstrated abnormally elevated LI, LI was diminished in right-onset male and left-onset male patients, while normal LI was found in left-onset male patients. A later study examined negative priming, which the authors assessed in a way that resembles how LI is usually measured in visual search paradigms (Filoteo, Rilling, & Strayer, 2002). In this study, controls reaction times increased when they had to search for a target that was previously a distractor; this effect was absent in chronically medicated patients with PD who were treated with multiple types of medications. Another study examined priming effects of distractor words in a lexical decision task (Marí-Beffa, Hayes, Machado, & Hindle,

2005). In a sample dominantly consisting of medicated PD patients, semantic priming was observed for distractor words, while such effects were absent in matched healthy controls.

In our study, we assessed LI, schizotypy, and processing of anomaly in two samples of patients with PD and in healthy controls (Thesis point 3, Polner et al., 2016). Anomaly processing was measured with a task adapted from a classical experiment in cognitive psychology (Bruner & Postman, 1949): participants were shown regular and trick playing cards (i.e. four of black hearts), and had to recognise the stimuli. Efficient processing of anomaly in this task has previously been associated with insight problem solving (DeYoung, Flanders, & Peterson, 2008), a cognitive process intrinsic to creativity (Arden et al., 2010; Dietrich & Kanso, 2010). We found that positive schizotypy, LI, and anomaly processing correlated with each other in the whole sample and also in every group. We have argued that the shared variance of these variables reflected exploration. Additionally, we have detected dose-dependent effect of DA drugs on these variables, suggesting that the way DA replacement therapy causes changes in cognitive functions can ultimately enhance creative potentials and induce psychotic experiences as well.

2.3.3 Individual differences in the neurocognitive effects of dopaminergic drugs

As we have seen previously, side effects of DA replacement therapy in PD (such as ICDs, psychoses, creativity and related behaviours) have heterogeneous prevalence, and they affect a variable and limited proportion of the patient population (Fénelon & Alves, 2010; Weintraub et al., 2010). Besides its significance in clinical work, predicting DA treatment's side effects before it is initiated could also provide valuable information to cognitive science about individual differences in the DA systems. In this section, we will overview research that examined individual variation in the cognitive effects of dopaminergic medications in healthy participants. Our overview will be restricted to data on how baseline cognitive control capacity and schizotypy can predict behavioural and neural response to drugs acting on the DA system.

The key principle in understanding such variation is that a drug effect on a system depends on characteristics of the drug and the baseline state of the system (Cools & D'Esposito, 2011). For instance, several studies have demonstrated that **working memory span** at baseline can predict the effect of DA agonists and antagonists on working memory (reviewed in Cools & D'Esposito, 2011). For instance, in those healthy participants who had relatively low working memory capacity (as indexed by the reading span task) before drug administration, a single dose of the DA D2 receptor agonist bromocriptine improved participants' performance on a test battery including measurements of working memory and executive functions. To the contrary,

performance on this test battery was impaired by bromocriptine in subjects who had higher working memory capacity at baseline (Kimberg, D'Esposito, & Farah, 1997). Furthermore, a study administered single doses of cabergoline (a D2 agonist) and haloperidol (a D2 antagonist) to healthy participants (Frank & O'Reilly, 2006). Importantly, baseline working memory span predicted the effect of these dopaminergic agents on several cognitive processes. For example, cabergoline impaired switching attention to a novel task-relevant set only in those participants who had high working memory capacity at baseline, while haloperidol made ignoring the previously relevant task set more difficult only for participants who had low working memory at baseline. Furthermore, improvement of learning from positive feedback after haloperidol was restricted to the low working memory group, while cabergoline induced a bias towards learning from negative feedback in the high working memory group.

Additionally, **schizotypy** has repeatedly been found to moderate the effects of dopaminergic drugs on cognitive performance and neural activity (reviewed in Mohr & Ettinger, 2014). A PET-study has found that schizotypy of healthy participants could predict the effect of d-amphetamine (an indirect DA agonist) on striatal DA release. More precisely, schizotypy scores predicted increase in DA release after drug administration in a brain cluster involving the head of the nucleus caudatus and extending to the ventral striatum. Moreover, drug induced DA release in the left frontal and parietal cortices were also predicted by total schizotypy scores. Follow-up analyses revealed that the associations were driven by the disorganised dimension of schizotypy (Woodward et al., 2011). In addition, schizotypy in healthy participants has been reported to modulate the effect of nicotine (an indirect DA agonist) and risperidone and amisulpride (DA antagonists) on eye movement control (Schmechtig et al., 2013). Risperidone increased antisaccade error rates only in medium schizotypy participants, while it did not have a significant effect on antisaccade error rate among high schizotypes. On the other hand, nicotine improved performance on the antisaccade task irrespective of schizotypy. Another study administered levodopa to healthy participants, and assessed turning bias, a putative indicator of hemispheric DA asymmetry (Mohr, Landis, Bracha, Fathi, & Brugger, 2004). It is assumed that turning is more likely to occur towards the hemisphere with the less active DA system. In the placebo group, positive schizotypy was associated with a preference to turn towards the left, while negative schizotypy tended to correlated with turning to the right. Curiously, the pattern of relationships between schizotypy dimensions and turning bias was reversed in the levodopa group, which might have indicated compensatory mechanisms working in healthy high schizotypes, the authors speculated.

In our study, we examined a group of cognitively intact patients with PD before their first lifetime DA medications, and after a twelve-week long follow-up period, during which the patients were receiving DA agonist monotherapy (Thesis point 4, Polner, Nagy, Takáts, & Kéri, 2015). A healthy control group was tested twice as well. We have found that DA agonists increased positive schizotypy and trait impulsivity, as indicated by self-report questionnaire scores. Divergent thinking assessed with a verbal task did not show any significant change at the group level. However, individual differences in change of verbal divergent thinking scores were predicted by baseline schizotypy and creative achievement. Positive schizotypy was related to change in originality, intelligence tended to be associated with change in fluency, and creative achievement and disorganised schizotypy were associated with change in flexibility. Our results could help identifying those patients with PD who are likely to enjoy the creative side effect of DA medication before the onset of treatment.

3. Concluding thoughts and further questions

We examined cognition and creativity in light of individual differences that are not only associated with exploration but also bear resemblance to mental disorders. We concentrated on schizotypy and ADHD-like traits in the general population (Thesis point 1 & 2), and on schizotypy in patients with PD (Thesis point 3 & 4). While the importance of DA appears rather obvious in the latter case, some researches have suggested dopaminergic involvement in schizotypy (Mohr & Ettinger, 2014; Woodward et al., 2011) and ADHD-like traits as well (Reuter et al., 2005; Tong et al., 2015).

First of all, in a review article we have argued that the association between schizotypy and creativity may be mediated by alterations of basic, dopamine-dependent cognitive processes (Thesis point 1, Polner & Kéri, 2015). We have highlighted some similarities and differences between schizotypy in the general population and openness, a robust predictor of creativity (Batey & Furnham, 2006). Future studies that simultaneously examine schizotypy and openness in healthy and clinical samples should explore the sources of the shared and the distinct variance of the two traits, and how they are shaped by alterations of dopaminergic neurotransmission. It also remains to be clarified whether schizotypy is differently associated with creativity in latent schizotypy subgroups of the general population (Hori et al., 2014; Kaymaz & van Os, 2010; Linscott & van Os, 2010).

A more detailed comparison of openness and positive schizotypy seems warranted for several reasons. It has been shown that the variance in openness that is independent of intellect is associated with positive schizotypy, while intellect and positive schizotypy has been found

to be negatively correlated (Chmielewski, Bagby, Markon, Ring, & Ryder, 2014; DeYoung et al., 2012). On the other hand, yet little is known about the variability in positive schizotypy that is independent of openness. Exploring the association of such variance with health and functional outcome might help separating aspects of schizotypy that call for intervention from those that could be the basis of personal growth (Tabak & Weisman de Mamani, 2013). Positive schizotypy has been shown to be associated with poor social and overall functioning, symptoms of depression and mania, suicide attempts, and impairment from alcohol and drug use (Kwapil et al., 2008; Kwapil, Gross, Silvia, & Barrantes-Vidal, 2013). Openness, to the contrary, emerged as a predictor of happiness and quality of life in a meta-analysis (Steel, Schmidt, & Shultz, 2008), and a study has reported that specific facets of openness – such as openness to feelings, actions, aesthetics, and ideas - were associated with reduced mortality in a sample of patients with cardiac disease (Jonassaint et al., 2007). Given the covariation between positive schizotypy and openness (Chmielewski et al., 2014; DeYoung et al., 2012), it would be of key importance to explore whether there are aspects of positive schizotypy that specifically predict the above adverse outcomes (Kwapil et al., 2008, 2013). Moreover, future research should attempt to separate the cognitive and neural correlates of the shared and non-shared variance of openness and positive schizotypy. For instance, reduced LI appears to be a common feature of these two traits (Kumari & Ettinger, 2010; Peterson & Carson, 2000; Peterson et al., 2002). On the other hand, openness has been associated with enhanced coupling of the right SN/VTA with the right dorsolateral PFC at rest and during perception of pleasant stimuli (Passamonti et al., 2015), whereas positive schizotypy was associated with reduced fronto-temporal white matter connectivity (M. T. Nelson et al., 2011) and reduced functional connectivity between the PFC and the amygdala during emotional reappraisal (Modinos, Ormel, & Aleman, 2010). Although none of these studies assessed positive schizotypy and openness jointly, they suggest that the two traits may have very distinct brain connectivity correlates.

Second, in a healthy adult sample drawn from the general population we found that ADHD-like like traits were weakly and negatively associated with inhibition-related functions (Thesis point 2, Polner, Aichert, et al., 2015). To our best knowledge, our study was the first to examine the relationship between ADHD-like traits and inhibition-related functions in a large sample of healthy adults in a laboratory setting. However, it should be highlighted that the associations between ADHD-like traits and inhibition-related functions appeared rather subtle. In addition, the effects might be specific to certain components of inhibition-related functions, as ADHD-like traits were predicted by performance only on two out of six well-established inhibition-related tasks. Latent variable modelling of ADHD-like traits and inhibition-related

functions could clarify if the detected associations are task-specific or indicate the contribution of a latent inhibition-related factor (N. P. Friedman & Miyake, 2004).

It should be added that ADHD is a highly heterogeneous disorder. Although subdimensions of ADHD-like traits and neuroticism were considered in our analyses, the existence of latent neuropsychological subgroups in the general population might have confounded the results. In an insightful study, Fair and colleagues (2012) investigated the heterogeneity of ADHD in a sample of nearly 500 children, 57 % of whom were diagnosed with ADHD. All the children were assessed with a complex neuropsychological test battery, which covered response inhibition, working memory, arousal, temporal information processing, memory span, response variability, and processing speed. Although at the group level, children with ADHD were impaired on all of the neuropsychological tasks, a classifier algorithm that attempted to predict ADHD diagnosis could not achieve satisfactory accuracy on the basis of test performance of the whole sample. Using community detection, the authors discovered latent subgroups both among typically developing children and among those with ADHD. Strikingly, the emerging subgroups among control and ADHD children had highly similar neuropsychological profiles: for example, a subgroup was detected in both samples that had increased response variability, and an additional subgroup with impaired response inhibition, working memory, memory span and output speed was detected in both samples. Crucially, response inhibition was deficient in only half of the ADHD subgroups. Underlining the clinical utility of the results, accuracy of diagnosis prediction on the basis of neuropsychological test scores was improved within latent subgroups, as compared to prediction in the entire sample.

The authors concluded that heterogeneity within ADHD appears to be nested within normal variability found in the typically developing population (Fair et al., 2012). On the whole, the study presented evidence showing that latent subgroups of children can be detected in the population, each of these groups is characterised by a distinct neuropsychological profile, and these latent subgroups are similar across typically developing children and children with ADHD. Although the above research was conducted with children, it seems logical that similar latent subtypes can be present in the adult population (Seidman, 2006), implicating that a simple continuum (Marcus & Barry, 2011) might not be the most precise representation of ADHD-related phenomena in the population. Future studies should apply data-driven latent subgroup detection in adult samples that involves healthy participants and patients with ADHD as well.

Although our study did not involve a measure related to creativity, the results are in line with findings of enhanced ideation but reduced idea evaluation in ADHD (e.g. White & Shah, 2011), which might demand lower and higher levels of cognitive control, respectively.

Moreover, as creative potential has been associated with efficient inhibition-related functions (Benedek et al., 2014; Edl et al., 2014), the meta-analytic negative correlation between ADHD and creativity (Paek et al., 2016) might reflect a disruptive net effect of deficient inhibition on creativity. Finally, one may argue that the impairment of inhibition-related functions associated with ADHD-like traits stems from unstable goal representations (Munakata et al., 2011), which can be considered to mirror a bias towards exploration instead of exploitation (Hauser et al., 2016). It remains to be investigated how the bias towards exploration in patients with ADHD (Hauser et al., 2016) is related to aspects of creativity.

Third, we found that dopaminergic therapy increased positive and disorganised schizotypy, reduced latent inhibition (LI), and improved anomaly processing in patients with Parkinson's disease in a dose-dependent fashion (Thesis point 3, Polner et al., 2016). These results suggest that the development of schizotypal traits in patients with PD during dopaminergic treatment co-occurs with specific alterations in cognitive processing that can also set the stage for the improvement of creativity. To our best knowledge, we have examined LI in medicated PD for the first time. Although at the theoretical level, LI, anomaly recognition and positive schizotypy all can be linked to exploration (DeYoung, 2013), examining patients with PD with a more direct and detailed measure of exploration would be fruitful. The exploration-exploitation trade-off can be examined during action choice based on expected reward values (Badre, Doll, Long, & Frank, 2012), or during visual and memory search (Hills, Todd, Lazer, Redish, & Couzin, 2015). Additionally, future studies might combine well-established computational models of reinforcement learning and attention in PD (e.g. Frank et al., 2004; Moustafa & Gluck, 2011) with neuroimaging methods to improve our understanding of exploration and creativity in PD. Finally, from our results it is not clear how DA therapy in PD affected automatic and goal-directed aspects of exploration (Gottlieb, Oudeyer, Lopes, & Baranes, 2013). Therefore, it remains to be clarified how creative abilities are mapped to various aspects of exploration.

The phenomenological description of schizotypy in PD represents another relatively uncharted territory. In our view, it would be important to examine whether increased schizotypal traits in PD, as indicated by elevated scores on self-report questionnaires, are qualitatively similar to or different from high schizotypy found in the general population. This question is especially intriguing given that hallucinations in PD usually have a neutral or even positive emotional tone (J. H. Friedman, 2013), while psychotic-like experiences reported by high schizotypes are usually distressing (Barrantes-Vidal, Chun, Myin-Germeys, & Kwapil, 2013; Kwapil, Brown, Silvia, Myin-Germeys, & Barrantes-Vidal, 2012). Moreover, it has been

demonstrated that methodological factors can largely influence the observed level of psychotic-like experiences (Linscott & van Os, 2010). In order to achieve a more detailed and accurate picture of schizotypy in PD, we suggest that more fine-grained methods (e.g. clinician interview or experience sampling) should be applied.

Our work might be compared to studies that investigated the cognitive correlates of frank psychosis in PD. For instance, in a recent study, psychosis in patients with PD was associated with impairments on the transitive inference task (Moustafa, Krishna, Frank, Eissa, & Hewedi, 2014). Given that interactions between the midbrain and the hippocampus have been shown to contribute to transitive inference (Shohamy & Wagner, 2008), the above findings imply abnormal hippocampal-midbrain interactions as putative neural substrates of psychosis in PD (Moustafa et al., 2014). Importantly, a series of rodent studies have demonstrated that connections between medio-temporal lobe structures (i.e. the hippocampus and the entorhinal cortex), the nucleus accumbens, and midbrain areas (i.e. the VTA) underpin LI (Schmajuk, 2005; Weiner, 2010). Therefore, the associations between reduced LI, positive schizotypy, and dopaminergic medication dosage (Polner et al., 2016) may suggest that abnormal midbrain-hippocampal interactions in PD are involved in subclinical positive schizotypy and in psychosis as well. However, this hypothesis remains to be tested with neuroimaging methods.

To date, a few studies have explored the neural correlates of visual hallucinations in PD. A group of researchers has reported elevated mean diffusivity in right posterior hippocampal regions in patients with PD who had minor visual hallucinations, as compared to patients without such complications (Yao et al., 2014). Additionally, patients with hallucinations had lower connectivity between the hippocampus and occipito-parietal and temporal areas, and reduced connectivity predicted visuospatial memory impairment. Interestingly, the severity of visual hallucinations were strongly correlated with visuospatial memory deficit. Another study reported reduced volume of the right cerebellar anterior vermis and the right precuneus in patients with PD who were experiencing minor visual hallucinations, relative to patients with PD who did not report hallucinations (Pagonabarraga et al., 2014). On the other hand, patients with minor hallucinations had greater grey matter volume in the left posterior lobe of the cerebellum and in the pars orbitalis of the left inferior frontal gyrus. In our opinion, functional and structural neuroimaging combined with separate evaluation of hallucination- and delusion-like positive schizotypal features (Hewitt & Claridge, 1989) in PD could reveal whether the above associations with neural structure and function are restricted to hallucinations in PD or generalise to positive schizotypy at a more global level.

Last but not least, we found that the improvement of creative potentials during DA agonist therapy in patients with PD was associated with pre-treatment schizotypy and creative achievement, while DA agonists generally increased positive schizotypy and trait impulsivity in the patients (Thesis point 4, Polner, Nagy, et al., 2015). These results implicate that flourishment of creative potentials might overlap with changes that lead to impulsive behaviour and psychotic-like experiences, as some previous studies have suggested (Joutsa et al., 2012; Kulisevsky et al., 2009; Schrag & Trimble, 2001). Our study can be seen unique in the literature in that patients with PD were assessed in a longitudinal design, which allowed identification of pre-treatment predictors of the DA agonists-induced improvement of divergent thinking. Future studies should examine whether increased divergent thinking in some patients with PD can predict more frequent engagement in creative activities and subsequent creative achievements (Jauk, Benedek, & Neubauer, 2013). Finally, how creativity gains meaning in the life stories of patients with PD (López-Pousa et al., 2012) seems to be a neglected but nevertheless important issue that remains to be investigated.

Besides informing basic and clinical cognitive neuroscience, our results might have relevance to the field of neuroenhancement. The possibilities of stimulating creativity with the tools of cognitive neuroscience have recently been enjoying the attention of several researchers. An intriguing line of studies that applied transcranial direct current stimulation (tDCS) to boost problem solving and divergent thinking in healthy participants has yielded promising results (Cerruti & Schlaug, 2009; Chi & Snyder, 2011; Chrysikou et al., 2013; Metuki, Sela, & Lavidor, 2012; Zmigrod, Colzato, & Hommel, 2015). Although it may appear that non-invasive brain stimulation studies represent the dominant neuroenhancement method to modulate creative thought, a pharmacological approach to improve creativity is far from novel. In the 1960s, several studies explored the potential of psychedelic drugs to improve creativity, mainly that of lysergic acid diethylamide (LSD), and anecdotal reports implicate that some artists and scientists also attempted to stimulate their creativity with LSD, with more or less success (see Fox, Girn, Parro, & Christoff, 2016; Sessa, 2008). Individual variation predicting the beneficial effect of LSD on creativity was one of the central questions. A study reported that those participants were likely to have enhanced creative thinking under LSD who ‘were able on free association, both to examine their internal perceptions (of affect and physical feelings) as well as sensitively observe their environment.’ (Zegans, Pollard, & Brown, 1967, p. 743). The authors of this study also noted that participants who improved ‘seemed to be the ones who had best handled real-life stress situations, most thoroughly and productively assimilated personal experiences, and had the least need to suppress or deny instinctual material.’ (Zegans et al.,

1967, p. 742). Although no psychometric scale was used in the above experiment, it is intuitively easy to see parallels between the quoted personality descriptions and modern conceptualisations of openness (DeYoung et al., 2012) and ego-resiliency (Farkas & Orosz, 2015). Importantly, both constructs have been associated with creative achievement (Batey & Furnham, 2006; Zabelina & Robinson, 2010) – and curiously, our data has shown that lifetime creative achievement can predict the emergence of creative potentials induced by dopaminergic drugs in patients with PD (Polner, Nagy, et al., 2015). Therefore, examining the role of openness and ego-resiliency in predicting creativity (and perhaps functional outcome) in longitudinal studies of patients with PD appears worthwhile.

Furthermore, exploring the mechanisms mediating the observed association between schizotypy and changes in divergent thinking could be an intriguing line of future research. One may speculate that the association could be due to highly schizotypal patients' more pronounced neural response to DA agonists (Woodward et al., 2011), and to their higher openness to novel ideas and unusual experiences (Chmielewski et al., 2014; DeYoung et al., 2012) that are induced by the dopaminergic drugs, which may contribute to the integration of these experiences and ideas into creative production, and a sense of "flow" (B. Nelson & Rawlings, 2010). Future psychopharmacological studies that apply personality assessment and experience sampling during creative thinking, perhaps combined with PET neuroimaging, may lead to a better understanding of the neurobiology and phenomenology of creativity.

All in all, our studies illustrate that the conceptual and methodological advancements related to the continuum theories of mental disorders are not only useful in interpreting the relationship between psychosis and creativity in the context of normal personality variation (Thesis point 1), and in exploring the ADHD-like trait correlates of individual variability in cognitive control (Thesis point 2), but they are also valuable in understanding subclinical psychotic-like features in PD (Thesis points 3 & 4). Self-report scales provide a feasible way of quantifying such features. However, as it has been discussed, self-report questionnaires have limited resolution (Linscott & van Os, 2010), and considering only the scores obtained with such scales might blur important qualitative differences between different variants of mental disorder-like phenotypes (Fair et al., 2012). For example, similar self-reported positive schizotypy scores could be obtained in a young adult who has been abused as a child and has excessively used cannabis in high school, and in a patient with PD who takes a high dosage of dopaminergic medications but neither did experience trauma nor did use drugs as an adolescent. Beyond differences in aetiology, the qualitative nature of schizotypy in these two fictive cases is likely to contrast (J. H. Friedman, 2013; Kwapil et al., 2012).

Beyond these methodological issues, some other limitations of the continuum theories of mental disorders should be mentioned. Similarly to what has been put forward with respect to creativity (Plucker et al., 2004), authors should precisely and explicitly define what they mean by "continuum" in the context of mental disorders (Linscott & van Os, 2010). With respect to our studies, following the terminology proposed by Linscott and van Os (2010), phenomenological continuity might exist between elevated positive schizotypy in PD and psychosis-spectrum disorders, as indicated by overlapping scores on self-report scales (Kocsis-Bogár, Nemes, & Perczel-Forintos, 2016). On the other hand, given that a remarkable amount of variance in positive schizotypy in PD was explained by dopaminergic medication dose in one of our studies (Polner et al., 2016), whereas positive schizotypy in the general population is modulated by several interacting factors of relatively small effect (van Os et al., 2008), continuity in terms of the underlying population structure seems unlikely.

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Appendix: the related studies

Study related to thesis point 1

Magyar Pszichológiai Szemle, 2015, 70. 3/3. 537–555.
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EGYÉNI KÜLÖNBSÉGEK AZ ALKOTÓ GONDOLKODÁSBAN: PSZICHÓZIS AZ ADAPTÍV MŰKÖDÉSBEN?*

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Célkitűzés: *A kreativitás összefüggést mutat a pszichotikus zavarok és a normalitás közötti átmenettel. A pszichózis spektrumon a szkizofrénia pozitív, negatív, dezorganizált és affektív tüneteire emlékeztető személyiségjegyek, a szkizotípiás vonások eltéréseit találjuk, melyek egészséges személyeknél összefüggést mutatnak az alkotókészséggel és az alkotó tevékenységekkel. Hogyan magyarázhatóak az összefüggések az alapvető megismerési folyamatok szintjén? Mely további egyéni különbségek relevánsak a kreativitás kérdésében?*

Módszertan: *Az áttekintésben olyan tanulmányokat dolgoztunk fel, melyek a kreativitást a pszichózis spektrum, illetve a személyiségvonások, kognitív képességek és társas tényezők mentén vizsgálták. Emellett szemléztünk a kérdéskör neurális oldalát célzó tanulmányokat is.*

Eredmények: *Bizonyos, az átmenetre jellemző neurokognitív vonások, mint a csökkent latens gátlás, az atipikus mintázatészlelés, valamint a szokatlan jelentőségtulajdonítás, köthetik a kreativitást a szkizotípia területéhez. Ezen funkciók mindegyikében a dopaminerg rendszerek érintettsége feltételezhető. A kreativitást a pszichotikusszerű jelenségekhez kapcsoló kutatások mellett az empirikus szakirodalom jelentős része hangsúlyozza, hogy a nyitottság, a magas intelligencia vagy a jól működő végrehajtó funkciók rendkívül fontosak a kreatív gondolkodásban és teljesítményben. További, az alkotótevékenységet fokozó tényezőnek mutatkozik a társas támogatás.*

Következtetések: *Az áttekintett irodalom alapján a szkizotípia neurokognitív szerkezete adaptív tényezőkkel társulva a kreativitás szolgálatába állítható. Az irodalom szintézise felveti a kérdést, hogy miként viszonyul egymáshoz az adaptív szkizotípia és a nyitottság felépítése és fejlődése.*

Kulcsszavak: *kreativitás, pszichózis, nyitottság, dopamin, intelligencia*

* A munka a Nemzeti Agykutatási Program (KTIA_NAP_13-2014-0020) támogatásával készült el.

A kreativitás és a mentális zavarok együttjárásáról szinte regénybe illő elképzelések élnek a laikus és a tudományos köztudatban (Jung, 2014). A kapcsolódás illusztrációjaként visszatérően hallhatunk híres művészek és tudósok vélt vagy valós lelki zavarairól (Dietrich, 2014). Mit üzennek az empirikus vizsgálatok a kreativitás és a mentális zavarok között feltételezett összefüggésről, különös tekintettel a legsúlyosabbnak tekintett pszichózisokra, amikor az egyén és a konszenzusokon alapuló valóság közötti kapcsolat megszakad?

A kreativitás alacsonyabb szintű kognitív folyamatok sokaságát foglalja magában (Abraham, 2014; Dietrich, 2004). Talán komplexitásából is adódik, hogy nincs egységesen elfogadott meghatározása, a kutatásokat olvasva rengeteg kreativitásdefinícióval szembesülünk (a kérdés történeti áttekintését adja Runco és Jaeger, 2012). Bár az elméleti (Dietrich, 2004, 2014) és módszertani sokszínűség (Arden, Chavez, Grazioplene és Jung, 2010; Dietrich és Kanso, 2010) nehezíti a tisztánlátást, a kutatók többnyire egyetértenek abban, hogy a kreativitás egy kettősség mentén ragadható meg. E konszenzus értelmében a kreatív aktus egy az adott társas közegben újnak, eredetinek, és egyben hasznosnak számító termék létrehozása, mely a képességek, a folyamatok és a környezet kölcsönhatásai által valósul meg (Pléh, 2010; Plucker, Beghetto és Dow, 2004; Sternberg, 2001). Figyelemre méltó, hogy a szabályozottság és a spontaneitás egyensúlyozása, mint kulcskérdés, a pszichoanalitikus kreativitáselméletekben is visszaköszön (Kővári, 2012).

A kreativitás rendszerszemléletű megközelítéseinek fő üzenete, hogy az alkotótevékenység megértéséhez rendkívül fontos az élettörténet, illetve a társas és a kulturális környezet figyelembevétele (Csíkszentmihályi, 2008; Pléh, 2010; Simonton, 2000). A társas tényezők közvetve jelennek meg Amabile (1983) elméletében, aki a kreativitás fő összetevőiként a belső motivációt, a szakértelmet, valamint a kreatív gondolkodási készségeket sorolta fel. A szociális közeg a belső motiváció serkentésén vagy elnyomásán keresztül befolyásolhatja az alkotótevékenységet (Amabile, Conti, Coon, Lazenby és Herron, 1996). Kaufman és Beghetto (2009) a kreativitás szintjeinek elkülönítését javasolták: elméletükben megkülönbeztetik a tanulás során felbukkanó új és értelmes értelmezéseket (mini C, mint creativity), a hétköznapi (kicsi C) és a professzionális (pro C) téren megvalósított újításokat, valamint a kiemelkedően kreatív, hírnévhez vezető alkotásokat (nagy C). Dietrich (2004) a kognitív és az érzelmi kreativitásra egy tartomány két végpontjaként tekintett. Bár az előbbi inkább a mérnöki-tudományos felfedezésekben érintett, az utóbbi pedig inkább a művészi alkotásban és a pszichoterápia alatt szerzett belátás folyamatában érvényesül, valószínű, hogy mindenféle kreatív tevékenység során a kognitív és érzelmi kreativitás eltérő arányban, de együttesen jut érvényre.

KREATIVITÁS ÉS LÉLEKTANI TERMÉSZETŰ EGYÉNI KÜLÖNBSÉGEK

Kreativitás a pszichózis spektrum kontextusában

A kreativitás változatos mentális zavarok kapcsán felmerült már mint a lelki sérülékenység egy lehetséges kedvező „mellékhatása". A fokozott alkotókészséget kapcsolatba hozták például a bipoláris hangulatzavarral (Kyaga és mtsai, 2011, 2013; Richards, Kinney, Lunde, Benet és Merzel, 1988; Simeonova, Chang, Strong és Ketter, 2005) vagy a hiperaktivitás-figyelemzavarral (Abraham, Windmann, Siefen, Daum és Güntürkün, 2006; White és Shah, 2011), bár az összefüggések korántsem egyértelműek (például Kyaga és mtsai, 2013; White és Shah, 2006). A kreativitás burjánzása jellemzően a pszichiátriai betegek egészséges elsőfokú rokonainál érhető tetten (Kyaga és mtsai, 2011, 2013; Richards és mtsai, 1988). A kreativitást a bipoláris hangulatzavarral, valamint az affektív temperamentummal összevetve elemző, kiterjedt szakirodalom bemutatása túlmutat jelen dolgozat keretein (például Andreasen, 1987; Janka, 2006; MacCabe és mtsai, 2010; Nowakowska, Strong, Santosa, Wang és Ketter, 2005; Rihmer, Gonda és Rihmer, 2006; Schlesinger, 2009); áttekintésünkben a pszichózisok és a kreativitás kérdéskörei közötti szövevényes viszonyrendszer feltárására fogunk törekedni.

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KREATIVITÁS ÉS LÉLEKTANI TERMÉSZETŰ EGYÉNI KÜLÖNBSÉGEK

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patológia és az alkalmazkodás között (Ettinger és mtsai, 2014; M. T. Nelson és mtsai, 2013). Változatos mérési szintekről származó adatok támogatják a szkizofrénia dimenzionális megközelítését (Ettinger és mtsai, 2014; Laurens, Hobbs, Sunderland, Green és Mould, 2012; Markon, Chmielewski és Miller, 2011; M. T. Nelson és mtsai, 2013; Rawlings, Williams, Haslam és Claridge, 2008a, 2008b), miszerint az egészséges populációban fellelhető pszichotikusszerű élmények és vonások valós átmenetet képeznek a normalitás és a pszichotikus zavarok között (de lásd még a kategorikus megközelítés mellett Beauchaine, Lenzenweger és Waller, 2008).

Egy 45 tanulmányt összegző metaanalízis a kreativitás, valamint a pozitív (a szkizofrénia pozitív tüneteire emlékeztető vonások) és a negatív szkizotípiás jegyek (a szkizofrénia negatív tüneteivel párhuzamos vonások) ellentétes irányú és gyenge összefüggéseire hívta fel a figyelmet (Acar és Sen, 2013). A metaelemzésbe bevont kutatások a kreativitást változatos úton mérték: egyes tanulmányok teljesítményteszteket (például divergens gondolkodás, asszociációs vagy mentális képzeleti tesztek), mások önjellemző skálákat (kreatív jellemvonásokat, kreatív szabadidős tevékenységeket vagy kiemelkedő kreatív teljesítményeket rögzítő kérdőívek) használtak. Az elemzés végkövetkeztetése szerint a pozitív és impulzív szkizotípiás jegyek tipikusan gyenge, pozitív kapcsolatot, míg a dezorganizált és negatív szkizotípiás vonások inkább gyenge, negatív összefüggést mutatnak az alkotókészséggel, annak mérési módjától függetlenül. Valamivel erősebb, de szintén gyenge összefüggést figyeltek meg a szkizotípia és a kreativitás között a művészet területén az általános kreativitáshoz képest, illetve a kiemelkedő alkotók körében a nem kiemelkedő személyekhez képest.

A már említett divergens gondolkodás teszteket gyakran alkalmazzák a kreatív potenciál felmérésére (Runco és Acar, 2012). E tesztek jellemzően egy sokféleképpen megközelíthető probléma megoldását kérik a vizsgálati személytől, például hogy fejezzen be egy néhány vonásból álló megkezdett rajzot vagy sorolja fel minél több felhasználási lehetőségét egy hétköznapi tárgynak. Az ötletek szokatlanságának és újszerűségének tendenciáját a szkizotípia pozitív, affektív és aszociális vetületéhez kötötték vizsgálatok (Claridge és Blakey, 2009; Zabelina, Condon és Beeman, 2014), míg az ötletek mennyisége a pozitív és dezorganizált szkizotípiás vonásokkal mutatott egyenes összefüggést (Folley és Park, 2005). A kreativitás megnyilvánulása az önjellemzésben, a személyiségben és a tevékenységekben a pozitív és impulzív szkizotípiás jegyekhez egyenesen, míg a dezorganizált jegyekhez fordítottan aránylott (Batey és Furnham, 2008). Továbbá dokumentálták a kreativitáshoz kapcsolódó hiedelmek, kiemelten a tudattalan folyamatokba vetett hit együttjárását a pozitív és dezorganizált szkizotípiás jegyekkel (Claridge és Blakey, 2009).

A pozitív szkizotípiás jegyek gazdagíthatják a művészi alkotás élményvilágát: egy kutatás szerint, melyben 100 művész vett részt, a pszichotikusszerű vonások összefüggtek az alkotás közben érzett különleges, izgalmas és élvezetes élményekkel, valamint az alkotásba való bevonódással (B. Nelson és Rawlings, 2010). Ez magyarázhatja azt az eredményt, miszerint 35, kiemelkedően kreatív képzőművész és zenész körében a pozitív szkizotípia magasabb szintje található, mint emi-

nens biológus és fizikus kutatók, valamint matematikusok ugyanekkora méretű csoportjában (RAWLINGS és LOCARNINI, 2008). Így valószínűnek tűnik, hogy a szokatlan élményeket inkább a művészi, mint a tudományos alkotómunkában lehet hasznosítani. Ugyanezen vizsgálatban a művészeti és a tudományos kreativitás elkülönülni látszott az asszociatív gondolkodás mintázatában: a művészekre a szokatlan képzettársítás, a matematikusokra és a fizikusokra inkább az ellentéteket összekötő gondolkodás volt jellemző egy szóasszociációs teszt alapján (RAWLINGS és LOCARNINI, 2008). A szkizotípia evolúciós szempontból adaptív lehet NETTLE és CLEGG (2006) tanulmánya szerint. Hobbi, elkötelezett és professzionális költők és képzőművészek (186 fő), valamint semmiféle kreatív tevékenységet nem végző személyek (239 fő) vettek részt vizsgálatukban. A hallucináció- és téveszmeszerű élmények pozitív kapcsolatot mutattak a kreatív aktivitás mértékével, az pedig pozitívan korrelált a szexpartnerek számával. Az impulzív-aszociális vonások az alkotótevékenységgel nem mutattak összefüggést, viszont egyenesen arányolottak a szexpartnerek mennyiségéhez.

Kreativitás az adaptív személyiségvonások és képességek kontextusában

Több tanulmány kísérelte meg a kreatív képességeket és teljesítményeket az adaptív személyiségműködés kontextusában ábrázolni. A Nagy Ötök (Big Five) személyiségmodell fogalmi keretei között dolgozó vizsgálatok szerint a kreativitás különféle mérései (divergens gondolkodás gördülékenysége és eredetisége, önjellemzés, illetve kreatív tevékenységek és teljesítmény) jellemzően fokozott nyitottsággal (KING, WALKER és BROYLES, 1996; MILLER és TAL, 2007; SILVIA és mtsai, 2008) és extraverzióval (FURNHAM és BACHTIAR, 2008; FURNHAM, BATEY, ANAND és MANFIELD, 2008; KING és mtsai, 1996), illetve esetenként alacsonyabb barátságossággal (FURNHAM és mtsai, 2008; KING és mtsai, 1996) vagy lelkiismeretességgel társulnak (SILVIA és mtsai, 2008). A nyitottságot és az extraverziót tömörítő *plaszticitás* szupervonás a kreativitás változatos mutatóival (például divergens gondolkodás, kreatív hobbik és teljesítmények, gyakorlatias és empatikus kreativitás) markáns pozitív kapcsolatokat mutatott (SILVIA, NUSBAUM, BERG, MARTIN és O'CONNOR, 2009). Ezzel szemben a lelkiismeretességet, a barátságosságot és a neuroticizmust (fordított) sűrítő *stabilitás* szupervonás a divergens gondolkodással (SILVIA és mtsai, 2008) és a való életben megnyilvánuló kreativitással közepes negatív, míg a tudományos-matematikai és a társas-empatikus kreativitással szerény pozitív összefüggésben állt (SILVIA és mtsai, 2009).

A mentális zavarok diagnosztikájának fejlesztése során újult lendületet kapott a törekvés a Nagy Ötök és a személyiségpatológia dimenziói, köztük a szkizotípia, integrálására (KRUEGER és MARKON, 2014). Ötfaktoros megoldással a nyitottság/intellektus és a különcség, valamint a szokatlan észlelések és hiedelmek egy latens változóra sorolódtak egyetemi hallgatókból álló mintákon (DE FRUYT és mtsai, 2013; THOMAS és mtsai, 2013). Bár alacsonyabb töltéssel, de ugyanezen a dimenzión jelentkezett a kockázatvállalás (DE FRUYT és mtsai, 2013) és az impulzivitás (THOMAS és mtsai, 2013), illeszkedve azon elképzeléshez, miszerint az affektív

diszreguláció szerves összetevője a szkizotípia jelenségkörének (Mason és Claridge, 2006). A nyitottság/intellektus vonásegyüttes pontos helye a pszichopatológia dimenzionális modelljében a nyitottság és az intellektus közös varianciájának statisztikai kontrollálása után nyilvánult meg. Ekkor a nyitottság pozitív, míg az intellektus vonás negatív kapcsolatot mutatott a szkizotípiás vonásokkal egészséges felnőttek (DeYoung, Grazioplene és Peterson, 2012) és pszichiátriai betegek körében is (Chmielewski, Bagby, Markon, Ring és Ryder, 2014), valószínűsítve, hogy a szkizotípia a nyitottság patológiás pólusának tekinthető.

Számos kutatás hangsúlyozta, hogy az alkotó gondolkodáshoz és tevékenységhez bizonyos személyiségvonások mellett magas intelligencia és jól fejlett kognitív kontroll is szükséges (áttekintésért lásd Barron és Harrington, 1981; Batey és Furnham, 2006). Lendületet adott a kreativitás kutatásának a 20. század közepén Guilford kritikai észrevétele, miszerint az intelligenciatesztek nem érzékenyek bizonyos, a kreativitáshoz szükséges adottságokra (Guilford, 1950). Klasszikus vizsgálatok szerint az intelligencia egy bizonyos küszöbig (IQ~120) együttjár a kreatív gondolkodási képességekkel, afelett pedig függetlenedik az IQ és az alkotókészség (például Barkóczi, Oláh és Zétényi, 1973; Getzels és Jackson, 1962). A divergens gondolkodás gördülékenységére (azaz az ötletek mennyiségére) és eredetiségére nézve megerősítette ezt a mintázatot egy vizsgálat, melyben közel háromszáz egészséges felnőttet vontak be. Ellenben a való életben elért kreatív teljesítmény és az IQ között töretlen egyenes összefüggést mutattak ki (Jauk, Benedek, Dunst és Neubauer, 2013). Az intelligencia szerepet játszhat még abban, hogy a kreatív gondolatok és cselekvések mások által is elismert teljesítményekhez vezessenek. Ugyanezen vizsgálati mintában az alkotótevékenységek gyakorisága a nyitottsággal és a divergens gondolkodással mutatott kapcsolatot, valamint összefüggésben állt a kreatív teljesítményekkel is. Az általános intelligencia egyrészt közvetlen kapcsolatban állt a kreatív teljesítményekkel, másrészt moderálta a kreatív tevékenységek és teljesítmények közötti összefüggést (Jauk, Benedek és Neubauer, 2013).

Az általános intelligenciának vajon mely komponensei igazán fontosak az alkotáshoz? Amabile összetevő-elmélete (1983) alapján feltételezhető, hogy a kreativitáshoz az összefüggések felismerésének képességére, valamint a szerzett ismeretekre-készségekre (fluid, illetve kristályos intelligencia; Cattell, 1987) egyaránt szükség lehet. A divergens gondolkodás eredetiségének intellektuális hátterének felderítésére számos vizsgálat törekedett. Körülbelül párszáz fős nagyságrendű, egyetemi hallgatókból álló mintákon végzett elemzések szerint a kiterjedt előhívási képesség (Beaty, Silvia, Nusbaum, Jauk és Benedek, 2014; Silvia, Beaty és Nusbaum, 2013), a kristályos intelligencia (Beaty és mtsai, 2014) és a távoli szemantikus asszociációk (Beaty és mtsai, 2014; Benedek és Neubauer, 2013) mind hozzájárulhatnak az originális ötletekhez. Újabb adatok szerint a kreatív divergens gondolkodás és a fluid intelligencia korrelációját nagyban a frissítési végrehajtó funkció és a nyitottság személyiségvonás magyarázza. Az eredeti és értelmes ötletek hátterében az automatikus válaszok gátlása és a reprezentációk frissítése bizonyultak lényeges végrehajtó folyamatoknak egy több mint kétszáz résztvevővel futtatott vizsgálatban (Benedek, Jauk, Sommer, Arendasy és Neubauer, 2014).

Egy ötven egyetemi hallgatóval végzett vizsgálat izgalmas eredményre vezetett: az eredeti divergens gondolkodáshoz és a kreatív teljesítményekhez nem a domináns válaszok gátlásának abszolút erőssége, hanem alkalmazásának rugalmas szabályzása járul hozzá (Zabelina és Robinson, 2010). Vagyis azok a személyek, akiknél nagymértékű gátlást lehetett mérni akkor, amikor várhatóan a nem domináns válasz volt a helyes, de kisebb gátlást, amikor nem számítottak arra, hogy szabályozniuk kell reakciójukat, nagyobb kreatív potenciállal és több kreatív teljesítménnyel rendelkeztek. Egy további tanulmányban, mely szintén félszáz egyetemi hallgatót vizsgált, az előhívás kiváltotta felejtési kísérletben mért emlékezeti gátlás fordított kapcsolatot mutatott az ötletelés eredetiségével és gördülékenységével (Lin és Lien, 2013). Tehát akiknél gyengébb volt a nem gyakorolt emléknyomokra irányuló elnyomás, azok több és egyedibb ötlettel álltak elő a divergens gondolkodási teszten.

Mindezek ismeretében érdemes kitérnünk arra, hogy számos metaanalitikus tanulmány pszichózisban gyenge kognitív kontrollról adott számot (például Dickinson, Ramsey és Gold, 2007; Lee és Park, 2005; Mesholam-Gately, Giuliano, Goff, Faraone és Seidman, 2009), illetve a pszichotikus betegek körülbelül kétharmadára alacsony intelligencia jellemző (Derks és mtsai, 2012; Dickinson és mtsai, 2007; Mesholam-Gately és mtsai, 2009). Valószínűsíthető, hogy magas intelligencia és ép kognitív kontroll hiányában a pszichózis azon sajátosságai, melyek adaptív tényezők társaságában kedveznek a kreativitásnak, egyéb maladaptív hatások mellett inkább rontják a társas készségeket és hátráltatják a mindennapi működést (Derks és mtsai, 2012; Fett és mtsai, 2011).

NEURÁLIS ALAPOK: A DOPAMINERG RENDSZEREK ELTÉRÉSEI

Milyen idegtudományi adatok állnak rendelkezésre az alkotókészség egyéni különbségeit illetően? Az elmúlt évtizedben a témában robbanásszerűen jelentek meg közlemények (összefoglalóért lásd Arden és mtsai, 2010; Dietrich és Kanso, 2010), ezért rövid áttekintésünkben a pszichózis elméleteiben központi szerepet játszó dopaminerg rendszerekre fogunk szorítkozni (Howes és Kapur, 2009).

Egy közel kétszáz egyetemista bevonásával készített feltáró viselkedésgenetikai kutatás a DRD4 dopamin receptor gént hozta összefüggésbe a figurális és verbális divergens gondolkodással (Mayseless, Uzefovsky, Shalev, Ebstein és Shamay-Tsoory, 2013). A vizsgálat eredményei szerint a gyengébb válaszgátlással összefüggésbe hozott DRD4 variáns (például Congdon, Lesch és Canli, 2008) társult kevesebb kreatív potenciállal. Egy másik feltáró tanulmány pedig a dopaminerg és a szerotonerg (Reuter, Roth, Holve és Hennig, 2006) rendszerekhez köthető gének polimorfizmusait jelölte meg a divergens gondolkodás eltéréseinek potenciális okozóiként. Ez a kutatás közel száz, az átlagosnál magasabb intelligenciájú egyetemistánál (átlag IQ~115) képi, szóbeli és matematikai problémák megoldása során mérte a képzeletgazdag, több szempontú gondolkodási képességet. Az ered-

mények szerint a DRD2 dopamin receptor gén alacsonyabb D2 receptorsűrűséggel társított variánsa (RITCHIE és NOBLE, 2003) kapcsolódott a fokozott kreatív potenciálhoz.

Ezzel összecsengő eredményt hozott az a kutatás, mely egy 14 fős, 59 éves átlagéletkorú mintán pozitron emissziós tomográfia (PET) segítségével mérte a D2 dopaminreceptor-sűrűséget. A talamusz receptorsűrűsége negatív együttjárást mutatott az ötletek mennyiségével a szóbeli, rajzolási és matematikai divergens gondolkodási teszteken. A striátumban és a frontális kéregben nem volt szignifikáns kapcsolat a D2 receptorsűrűség és a kreatív potenciál között. Lehetséges, hogy a talamikus kapuzástól függően csökken a prefrontális kérgi jel-zaj arány, ami kedvez a kreatív gondolattársításoknak (DE MANZANO, CERVENKA, KARABANOV, FARDE és ULLÉN, 2010). Egy másik kutatócsoport strukturális mágneses rezonancia képalkotást (magnetic resonance imaging, MRI) bevetve agyi régiók térfogatát korreláltatta egy összesített divergens gondolkodási indexszel, mely magában foglalta az ötletek mennyiségét, eredetiségét, kidolgozottságát és változatosságát. A vizsgálatban részt vevő félszáz fiatal felnőttnek (átlagéletkoruk 22 év) minél több válasszal kellett előállniuk olyan kérdésekre, mint például „Mire lehet használni egy újságot az olvasáson túl?", vagy „Mi jellemez egy jó TV-készüléket?", illetve „Mi lenne, ha a világ összes egere eltűnne?". A dopaminerg rendszerekhez tartozó középagyi, kéreg alatti és kérgi területek térfogata pozitív kapcsolatban állt az összesített divergens gondolkodási indexszel (TAKEUCHI és mtsai, 2010). E néhány feltáró vizsgálat eredményei kétségtelenül izgalmasak, de vajon milyen alapvető kognitív folyamatok által kapcsolódhatnak a kreativitás jelenségköréhez a dopaminerg rendszerek?

Dopaminfüggő alapvető kognitív folyamatok és egyéni különbségeik

A dopaminerg rendszerek gyógyszeres manipulációjára a latens gátlás érzékenységet mutat (LUBOW, 2005; SWERDLOW és mtsai, 2003; WEINER és ARAD, 2009). Latens gátlás alatt azt a jelenséget értjük, amikor egy inger ismételt, következmények nélküli bemutatásának hatására később ezen ingerrel nehezebben történik meg az asszociatív tanulás. A latens gátlás a feldolgozás hangsúlyát a régi és nem fontos ingerek felől az újak irányába tolja el, ezáltal szorosan összefonódik a szelektív figyelem működésével (LUBOW, 2005). A pozitív szkizotípiás jegyekkel a latens gátlás jellemzően fordított összefüggésben áll (BURCH, HEMSLEY, PAVELIS és CORR, 2006; GRANGER, PRADOS és YOUNG, 2012; TSAKANIKOS, SVERDRUP-THYGENSON és REED, 2003), bár a hatások gyengék és nem mindig mutathatóak ki (például EVANS, GRAY és SNOWDEN, 2007). További vizsgálatok arra utalnak, hogy magas szkizotípiás személyeknél a latens gátlás kiépülése ép, azonban kifejeződése abnormális (TSAKANIKOS és REED, 2004). Mások felvetették, hogy a hiányos latens gátlás elsősorban a szorongással és nem a szkizotípiás jegyekkel áll összefüggésben (BRAUNSTEIN-BERCOVITZ, RAMMSAYER, GIBBONS és LUBOW, 2002).

A dopaminerg neurotranszmisszió kitüntetett jelentőséggel bír továbbá a predikciós hiba jelzésében (SCHULTZ, 2000), mely a várt és a tényleges események

közötti eltérést kódolja (FIORILLO, TOBLER és SCHULTZ, 2003). Az emberi striátumban mért predikciós hiba érzékeny a dopaminerg rendszerek gyógyszeres manipulációjára (PESSIGLIONE, SEYMOUR, FLANDIN, DOLAN és FRITH, 2006). A neurális számítások szintjén a predikciós hiba összesítve jelzi egy esemény váratlanságát és jelentőségét (SMITH, LI, BECKER és KAPUR, 2006). A predikciós hiba részt vesz a belső modellek és a külvilág kölcsönhatásainak szabályzásában: ezen folyamat révén formálják a tapasztaltak a világról alkotott képet (CARHART-HARRIS és FRISTON, 2010; FRISTON, 2009). A rendszer zavara esetén a belső reprezentációk és a világ összhangja megbomlik: a személy a valóságtól „elcsúszik", hallucinációk és téveszmék bukkannak fel az élményvilágban (FLETCHER és FRITH, 2009). Egészséges személyeknél a mágikus gondolkodással a striátumban mért predikciós hiba együttjárt egy vizsgálatban. A téveszmeszerű gondolatok keltette szorongás viszont inkább a jobb dorzolaterális prefrontális kéregben mért predikciós hibával állt összefüggésben (CORLETT és FLETCHER, 2012), hasonlóan a klinikai pszichózis esetén megfigyeltekhez (CORLETT és mtsai, 2007). Az eredmények arra utalnak, hogy a mentális egészséget károsító delúzió és az „egészséges" szkizotípiás élmények neurális lenyomata különbözik (CORLETT és FLETCHER, 2012). Egy izgalmas nyitott kérdés, hogy a predikciós hiba eltérései miként kapcsolódnak az alkotó gondolkodáshoz.

Az elvárások és tapasztalatok összehangolásának anomáliáit tükrözheti, hogy magas pozitív szkizotípiás személyek hajlamosak értelmet észlelni véletlen szerveződésű, értelmetlen ingerekben (DEYOUNG és mtsai, 2012). A téveszme- és/vagy hallucinációszerű élményekről beszámoló egészséges személyek fogékonyak arra, hogy értelmetlen karakterláncokban értelmes szavakat észleljenek (GRANT, BALSER, MUNK, LINDER és HENNIG, 2014; REED és mtsai, 2008; TSAKANIKOS, 2006; TSAKANIKOS és REED, 2005), háromszögek véletlenszerű mozgását szabályosnak ítéljék és a háromszögeknek szándékot tulajdonítsanak (FYFE, WILLIAMS, MASON és PICKUP, 2008), vagy vizuális (SIMMONDS-MOORE, 2014) és auditoros zajban értelmes észleleteket tapasztaljanak meg (GALDOS és mtsai, 2011; SIMMONDS-MOORE, 2014). Ezek a tendenciák kedvezőtlen esetben pszichotikus tünetekhez vezethetnek (például GALDOS és mtsai, 2011), de akár utat nyithatnak kreatív meglátásoknak: aki képes rendszert látni abban, ami mások számára véletlenszerű zaj (DEYOUNG és mtsai, 2012; FYFE és mtsai, 2008; GRANT és mtsai, 2014), az új összefüggéseket fedezhet fel (MEDNICK, 1962).

A pszichotikus tünetek hozadékai lehetnek a jelentőség nélküli információ sikertelen elnyomásának, majd az ebből fakadó önkényes képzettársításoknak (HOWES és KAPUR, 2009; B. NELSON, WHITFORD, LAVOIE és SASS, 2014). A jelentőségtulajdonítás aberrációja nem korlátozódik a klinikai pszichózisokra, a szkizofréniaszerű szubklinikus jelenségekkel is összefüggést mutat (ROISER és mtsai, 2009; SCHMIDT és ROISER, 2009). Parkinson-kórral diagnosztizált betegek dopamin agonista terápiája során az adaptív és aberráns jelentőségtulajdonítás egyaránt erősödést mutatott vizuális reakcióidő feladatban, ahol a helyes válaszadást jutalmazták. Az illuzórikus együttjárások önkényes kialakulása összefüggésben állt a hallucináció- és téveszmeszerű élmények enyhe fokozódásával (NAGY és mtsai, 2012). A jelentőségtulajdonítás torzulásai nyomán a pszichózis spektrumon a

konszenzuális értelmezések kevésbé jutnak érvényre, megzavarván az illeszkedést a fizikai és a társas környezethez (B. Nelson és mtsai, 2014). A kontextuális szabályzás szelídülése azonban segítheti a kreatív megoldást olyan esetekben, amikor a standard elvárások nem célravezetőek.

Pszichotikusszerű neurokognitív vonások adaptív konstellációkban támogatják a kreativitást

Figyelemre méltó, hogy az adaptív személyiségvonások közül a szkizotípiához közel álló nyitottság (DeYoung és mtsai, 2012), illetve az extraverzió is alacsony latens gátlással társul (Peterson és Carson, 2000; Peterson, Smith és Carson, 2002). A nyitottság egy tendenciát jelez arra, hogy az egyén szenzoros és absztrakt információt keressen, feldolgozzon és hasznosítson (DeYoung, 2014). Fokozott nyitottságú személyek dorzolaterális prefrontális kéregre érzékeny neuropszichológia tesztek szerint hatékonyabb kognitív kontrollal (DeYoung, Peterson és Higgins, 2005), illetve magasabb verbális intelligenciával bírnak (DeYoung, Quilty, Peterson és Gray, 2014). A nyitottság egyéni különbségeit nemrég összefüggésbe hozták a prefrontális kéreg dopaminellátottságában központi szerepet játszó gének polimorfizmusaival (DeYoung és mtsai, 2011). Tehát a magas nyitottságban együttesen jelennek meg a való életben elért kreatív teljesítményhez szükséges tényezők, úgymint az alacsony latens gátlás és a magas intelligencia (Kéri, 2011).

Egy friss kutatás rejtett profilelemzéssel adaptív és maladaptív magas szkizotípiás, illetve adaptív alacsony szkizotípiás csoportokat mutatott ki egészséges középkorú felnőttek körében (Hori és mtsai, 2014). Mindkét magas szkizotíp csoportban gyakoribbak voltak az észlelési és gondolkodási aberrációk. Az adaptív csoportnál az érzelemszabályozás, az önirányítottság, illetve a társas és a kognitív funkciók terén nem jelent meg az a finom károsodás, ami a maladaptív szkizotípiás csoportot jellemezte. Emellett kiugróan magas spiritualitás jellemezte az adaptív magas szkizotípiás csoportot. Az alkotó gondolkodás vizsgálatára sajnos nem terjedt ki ez a kutatás.

ÖSSZEGZÉS

Zsenialitás vagy patológia?

Izgalmas kérdés, hogy milyen tényezők határozzák meg, hogy a pszichotikusszerű vonások a fokozott alkotókészség vagy a mentális zavarok szolgálatában állnak. Jelentős szerepe lehet az egymással kölcsönhatásba lépő genetikai faktoroknak és fejlődési hatásoknak (Alemany és mtsai, 2014; van Os és mtsai, 2008), valamint a traumatikus eseményekkel való megbirkózás képességének, a rezilienciának (Tait, Birchwood és Trower, 2004). Nem elhanyagolható továbbá a jó kognitív képességek, az adaptív személyiségtényezők és a spiritualitás hatása, amelyek lehetővé

teszik a pszichotikusszerű élmények biztonságos keretezését (Hori és mtsai, 2014; Schofield és Claridge, 2007). A stresszorok fokozzák a pszichotikusszerű tünetek és a paranoid gondolatok átélésének valószínűségét, különösen azoknál, akiknél kifejezettek a pozitív szkizotípiás jegyek (Barrantes-Vidal, Chun, Myin-Germeys és Kwapil, 2013). Képalkotó vizsgálatok érdekes módon a dopaminrendszer stresszre mutatott válaszkészségét a negatív szkizotípiás vonásokkal és a szkizofrénia hajlam egy biológiai markerével kapcsolták össze (Soliman és mtsai, 2008, 2011). A társas támogatás segíthet a fejlődést adaptív mederben tartani (Domínguez-Martínez, Medina-Pradas, Kwapil és Barrantes-Vidal, 2014), fokozván egyúttal a kreativitás kibontakozását is (Amabile és Pillemer, 2012; Kéri, 2011).

A szkizotípiára jellemző neurokognitív sajátosságok növelhetik a kreativitást, amennyiben olyan adaptív tényezők kísérik őket, mint a magas intelligencia, a fejlett kognitív kontroll vagy a jó társas készségek. Következésképp a kreativitás nem a patológiás, hanem elsősorban az egészséges lelki működés velejárójának tekinthető. A kreativitás kutatásában a kognitív idegtudományi megközelítés adta ismeretek értékesek, önmagukban azonban korlátozottan értelmezhetőek, tágabb – élettörténeti, társas, kulturális – kontextusba ágyazásuk izgalmas jövőbeni iránya lehet a kérdéskör vizsgálatának. Emellett a szkizotípia és a magas nyitottság felépítése és fejlődése közötti eltérések, illetve átfedések is tisztázásra várnak. Ezeknek ismeretében nem csupán a kreativitás és a mentális zavarok összetettségének mélyebb megértése válna lehetővé, de egyúttal akár a pszichózis megelőzése is új szempontokkal gazdagodhatna.

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INDIVIDUAL DIFFERENCES IN CREATIVE THINKING: PSYCHOTIC-LIKE FEATURES IN AN ADAPTIVE CONTEXT?

POLNER, BERTALAN – KÉRI, SZABOLCS

Rationale: *Creativity can be related to the continuum between psychotic disorders and normality. Schizotypal traits, that is, personality traits resembling the positive, negative, disorganized and affective symptoms of schizophrenia, have been associated with creative potential and achievement in healthy populations. How can we explain these relationships at the level of fundamental cognitive processes? What are the other individual differences relevant to creativity?*

Method: *We reviewed studies that investigated creativity either in the context of the psychosis spectrum or in relationship with personality traits, cognitive abilities, and social context. Additionally, studies examining potential neural correlates of creativity were discussed in the review.*

Results: *Reduced latent inhibition, atypical pattern perception and aberrant salience are some neurocognitive features characterizing the psychosis spectrum which might provide a link between schizotypy and creativity. Dopaminergic involvement has been assumed in all of these functions. On the other hand, a substantial part of the empirical literature underscored the crucial role of openness, high intelligence and intact executive functioning in creative thinking and achievement. Additional studies highlighted the importance of social support in the creative process.*

Conclusions: *The reviewed literature suggests that the neurocognitive structure of schizotypy, when accompanied by adaptive factors, can subserve creativity. The precise nature of the relationship between the features and the development of adaptive schizotypy and openness remains to be clarified.*

Key words: *creativity, psychosis, openness, dopamine, intelligence*

Study related to thesis point 2

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ORIGINAL PAPER

Gently restless: association of ADHD-like traits with response inhibition and interference control

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Abstract Impairment of inhibition-related functions is one of the most pronounced cognitive deficits found in attention-deficit/hyperactivity disorder (ADHD). Compelling evidence from studies of unaffected relatives of patients with ADHD and of ADHD-like traits in healthy subjects suggest the continuous distribution of ADHD symptoms in the population. A more subtle inhibitory deficit can also be found in healthy relatives of patients and in subjects with high ADHD-like traits. Here, we examined the relationship between inhibitory performance and ADHD-like traits, for the first time, in a large sample of healthy adults by applying multiple, widely used tests of inhibition-related functions. ADHD-like traits, in general, were independently predicted by Stroop interference score and, at trend level, by go/no-go commission error rate while controlling for socio-demographic factors, verbal intelligence and neuroticism. Additionally, higher inattentive traits were related to worse Stroop performance at trend level, and higher hyperactive/impulsive traits were significantly associated with more go/no-go commission errors. ADHD-like traits were strongly related to neuroticism. The study shows that individual differences in ADHD-like traits are related to variance in fundamental inhibition-related functions over and above effects of negative affect regulation, but the relationships tend to be small. The results suggest the quasi-dimensionality of ADHD and raise further questions about the relationship between genetic factors and the deficit of inhibition-related functions in the ADHD spectrum.

Keywords ADHD · Inhibition · Interference control · Continuum · Neuroticism

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) [1] shows substantial heritability [2] and has a worldwide prevalence of approximately 5 % among children and adolescents [3] and of approximately 3 % among adults [4]. ADHD is characterized by abnormal structural and functional connectivity of brain networks playing key roles in executive functions [5, 6], that is, higher-order mental processes regulating cognition and behavior [7].

Inhibition, one of the most widely studied executive functions [7, 8], refers to the ability to suppress irrelevant stimuli, information or responses in a goal-directed manner [7, 9–11]. Inhibition is a broad, multi-faceted concept, covering different aspects of cognitive functions [12]. *Prepotent response inhibition* is the ability to preclude the execution of dominant responses [10, 12], whereas *response cancellation* is the ability to halt an already initiated response [9, 13]. *Interference control* [10–12] is the

ability to resolve interference occurring due to distracting stimuli [14] and competing responses [15]. In this paper, we will refer to these related constructs as *inhibition-related functions* [12].

It has been proposed that a deficit in inhibition-related functions is a core component of ADHD [10], although impairments are observed in other cognitive domains as well [16–18]. Patients with ADHD demonstrate decreased performance on inhibition-related tasks such as the stop-signal task [18–23], the Eriksen flanker and the Simon task [24], the antisaccade task [25–28], the go/no-go task [29, 30] and, somewhat controversially, the color-word Stroop task [20, 31–35]. Similar inhibition-related deficits are also present, to a lesser extent, in unaffected siblings [36–40] and parents [38] of patients with ADHD, implicating a genetic component behind the dysfunction. Unaffected relatives are important to study as they provide evidence for a continuum of ADHD-like traits ranging from patients to healthy people with no close family members diagnosed with ADHD. These findings suggest that impaired inhibition-related functions can be regarded as endophenotypes of ADHD [41], i.e., a trait marker of the genetic vulnerability for the disorder [42], persisting regardless of clinical status [43]. Shared heritable influences on inhibition-related functions [13, 44] and ADHD-like traits are indicated by twin studies [45, 46]. ADHD-like traits and inhibition-related functions show within-subject correlation during development [46, 47], but no parent–offspring correlations have been found between them [48].

ADHD-like traits differ from inhibitory deficits as they manifest a subclinical expression of the clinical phenotype of ADHD in the normal population [45, 49–52]. In contrast to neurocognitively assessed endophenotypes [41], such traits are measured with various rating scales in the normal population [53, 54]. They have been related to polymorphisms in genes associated with the dopaminergic and serotonergic systems [53]. Mirroring the DSM-IV classification of ADHD [1], ADHD-like traits can be divided into the overlapping, but separable subdimensions of inattention and hyperactivity/impulsivity [55, 56], which map somewhat differentially to temperament and executive functions [57]. Partially differing etiologies of inattention and hyperactivity/impulsivity [58–60] cause separable developmental pathways of these dimensions [61].

Higher ADHD-like traits are associated with less efficient inhibition-related functions among children and adolescents drawn from the general population [45, 62]. In healthy adults, higher ADHD-like traits are associated with subtle forms of neurocognitive deficiencies frequently reported in ADHD [63–66], while one study reported a rather controversial pattern of relationships between ADHD-like traits and inhibition-related functions [67]. These studies suggest that at least some of the cognitive and neural deficits in ADHD are not exclusively associated with the illness per se. Instead, the findings suggest that proximity to ADHD, indexed either through genetic relatedness or through high ADHD-like traits, can be observed in the general population and covaries with some of the deficits observed in the clinical condition.

A dimensional model of ADHD gains further support from a recent meta-analytical study [50], which demonstrated that dimensional models of psychopathology in general are more valid and reliable than discrete approaches. The latent dimensional structure of ADHD symptoms in the population [51] has also gained empirical support from a taxometric study [49], and dimensional representation of ADHD symptoms can be useful in clinical decision making [68].

In this study, we aimed to investigate in detail the relationship of a comprehensive battery of inhibition-related measures [69] with ADHD-like traits in a large, healthy adult sample. To our knowledge, no such study has previously been reported. As our goal was to detect variation in inhibition-related functions *specifically* related to ADHD-like traits, we statistically controlled for neuroticism in this relationship as it is not only associated with various forms of psychopathology, but it is related to psychopathology-like traits in healthy volunteers [70, 71]. We reasoned that significant relationships between ADHD-like traits and performance would identify those cognitive functions that are sensitive to a dimensional vulnerability to ADHD.

Method

Participants

Participants were recruited through circular emails and newspaper and local community advertisements. All participants were required to be aged 18–55 years and German native speakers. Exclusion criteria were (a) any current DSM-IV Axis I disorders (using the German version of the Mini-International Neuropsychiatric Interview; [72], (b) a past or current diagnosis of ADHD, (c) any diagnoses of psychotic disorders or ADHD among first-degree relatives, (d) a history or evidence of neurologic disorders, (e) any current physical condition, (f) any current consumption of over-the-counter or prescription medication (except for contraceptives), and (g) any visual impairments (other than the use of corrective lenses or glasses). Demographic data on age, gender and years spent in full-time education were acquired with a questionnaire. Ethical approval was obtained from the ethics committee of the Faculty of Medicine of the University of Munich. Participants provided written informed consent and were reimbursed for

Table 1 Descriptive statistics of psychometric and inhibition variables

Measurement	Mean (SE)
MWT-B	30.69 (0.14)
Neuroticism sum score	16.28 (0.37)
ASRS sum score	22.42 (0.38)
Antisaccade error rate (%)	27.11 (0.85)
Go/no-go commission errors (%)	23.66 (0.65)
Stop-signal reaction time (ms)	179.82 (3.40)
Stroop interference score (s)	40.42 (0.55)
Eriksen flanker interference score (ms)	52.60 (1.08)
Simon interference score (ms)	62.77 (1.46)

Legend: Data indicate means, with standard error of mean in parentheses

MWT-B Mehrfachwahl-Wortschatz-Intelligenztest, *ASRS* Adult ADHD self-report scale

their time and effort. After screening participants according to inclusion criteria and the below described outlier removal procedure, the remaining final sample included 440 participants (234 males). Their average age was 26.18 years ($SE = 0.33$; minimum = 18; maximum = 52), and they had completed an average of 15.87 years ($SE = 0.11$) in full-time education (see Table 1 for further descriptive statistics).

Psychometric assessment

ADHD-like traits were assessed with the German version of the Adult ADHD Self-Report Scale (ASRS [73]; adapted to German by [53]. The ASRS comprises of 18-items and is based on the DSM-IV-TR ADHD criteria [1]. Each item measures the frequency of a symptom, asking respondents to indicate how often it occurs (0 = *never*; 4 = *very often*). Based on the ASRS sum score, the likelihood of having ADHD can be estimated (<34: unlikely, 34–46: likely, 46<: highly likely). The ASRS has a two-factorial structure with an inattention scale (9 items, Cronbach's alpha = 0.75) and a hyperactivity/impulsivity scale (9 items, Cronbach's alpha = 0.77) with good reliabilities in the original study (Cronbach's alpha for the total ASRS = 0.82) [53]. In our study, comparable reliabilities were observed (0.76 for inattention, 0.74 for hyperactivity/impulsivity and 0.82 for the total ASRS).

Neuroticism was measured with the German version of the NEO-FFI [74]. The scale consists of 12 items and participants are requested to respond using a five-point Likert-type format (*strongly disagree* = 0; *strongly agree* = 4). The neuroticism subscale had good internal reliability (Cronbach's alpha = 0.86) in our study.

Verbal intelligence was assessed using the German test MWT-B (Mehrfachwahl-Wortschatz-Intelligenztest; [75, 76]). The MWT-B includes 37 rows in increasing difficulty each containing one real word among four non-words. Participants have to identify and mark the real word. Every correct answer is coded with 1, wrong or missing answers are coded with 0. The maximum score thus is 37. Reliability of the MWT-B was satisfactory in this sample (Cronbach's alpha = 0.67). Four participants scoring 20 or less on the MWT-B (comparable to an IQ value of 77) were excluded from further analysis.

Cognitive assessment

Participants were tested individually, in a quiet, darkened room. The tasks were presented in random order to exclude systematic order effects. The computerized tests were presented on a 17-inch monitor. The paper-and-pencil-based Stroop task was carried out on a table. Immediately before the experimental sessions, the participants completed practice trials during which the experimenter ensured that the instructions had been understood by the participant.

Antisaccade task

Head movements were minimized by the application of a chin rest with a distance from eye to screen of 57 cm. The eye tracker was always calibrated with a nine-point calibration task before the antisaccade task commenced. The visual stimulus was a black circle (approximately 1° of visual angle in diameter) shown on a white background. The antisaccade task was programmed using the SR Research Experiment Builder software [77].

The task involved 60 step trials (no gap, no overlap). A trial consisted of the target in the central position ($x = 0°$, $y = 0°$) for 1,000–2,000 ms and, subsequently, at one of four possible positions ($x = \pm 7.25°$, $y = 0°$ and $x = \pm 14.5°$, $y = 0°$), each of which was used 15 times. Participants were required to look at the central target and to perform a horizontal saccade to the opposite position of a peripheral target. Participants were instructed to look as fast and spatially accurately as possible to the mirror image location of the peripheral target while avoiding a prosaccade toward the target.

Right eye movements were recorded using a combined corneal reflection and pupil tracker (EyeLink 1000, SR Research, Kanata, Ontario, Canada) at a sampling frequency of 1,000 Hz. Eye movement analysis criteria were a minimum amplitude of 1° and a minimum latency to stimulus of 80 ms. Saccades were identified using the semi-automated software package Data Viewer (SR Research) and individually verified by a rater. The percentage of directional errors was the dependent variable. A directional error occurred when the first valid saccade

following target onset was made in the direction of the target. Because of calibration problems or poor signal quality, data of seven participants were missing. Participants performing the task with a directional error rate of 80 % or more were excluded from further analyses ($N = 26$).

Stroop task

Participants completed the well-validated German language Stroop task [78]. This paper-and-pencil test has three conditions. In the first condition, participants were asked to read out color words, in the second to name color bars (four different colors: red, yellow, green and blue) and finally, in the interference condition, they were instructed to name the ink color of color words. The German words "ROT" (red), "GELB" (yellow) "GRÜN" (green) or "BLAU" (blue), printed in a contrasting color (either red, yellow, green or blue), were presented to participants in the interference condition. The three conditions were divided into nine different blocks of 72 items each. The three conditions were always presented in the above-mentioned order, and the sequence of the nine blocks remained the same for all participants. Participants were instructed to maximize speed and accuracy. A stopwatch was used to record the time required to complete the single blocks. The dependent variable was the interference score, which was calculated by subtracting the median reaction time of the interference condition from the median reaction time of the word reading condition. Two participants, who cheated in the interference condition and one participant with an extremely slow reading speed, were excluded from further analysis.

Stop-signal task

A stop-signal task version from the M.A.R.S. battery developed by Rubia et al. [30] was applied in this study. In go-trials, a green airplane (13 cm width × 6 cm height) appeared for 1,000 ms pointing either to the left or to the right. The airplane was followed by a black screen lasting for 700 ms. In stop-trials, the presentation of the airplane was followed by the stop-signal—an exploding bomb—which was presented initially 250 ms after the onset of the go-signal (the airplane) and lasted for 300 ms. Participants were instructed to press the arrow key matching the airplane's pointing direction and to halt their ongoing response in the case of an explosion. The task involved 178 trials of 1,700 ms duration; 130 were go-trials (equal probabilities for each direction) and 48 were stop-trials (equal probabilities of stop-signals appearing either after a left or right pointing airplane).

A tracking procedure was included in this version of the task (see [23]) which guaranteed that participants successfully inhibited on approximately 50 % of the stop-signal trials. This was achieved by dynamically adjusting the interval between the go-signal and the stop-signal (called stop-signal delay). If the percentage of inhibition, which was recalculated after each stop-trial, was higher than 50 %, the task was made more difficult so that the stop-signal delay was lengthened by 50 ms in the next stop-trial; if the percentage of inhibition was lower than 50 % the stop-signal delay was shortened by 50 ms in the next stop-trial to make the task less difficult. This tracking procedure thus leads to a stop-signal delay at which participants inhibit their response in approximately 50 % of trials. On this stop-signal delay, the stop process (the latency of inhibiting the already initiated response) and the go process (finishing the initiated response) finish on average at the same time. The stop and the go process are assumed to be independent from one another, and what actually happens in one specific trial (successfully inhibiting vs. responding) depends on random variation. As this critical stop-signal delay corresponds to the point in time at which the stop process finishes, this information can be utilized to estimate the stop-signal reaction time (SSRT). The outcome of each trial depends on three factors (go reaction time, stop-signal delay, and SSRT) and two of them (go reaction time, stop-signal delay) can directly be measured. As participants inhibit successfully in half of the stop-trials at the critical stop-signal delay, SSRT plus stop-signal delay must equal mean go reaction time. Thus, SSRT can be calculated by subtracting stop-signal delay from mean go reaction time [23].

The SSRT was the dependent variable. SSRT scores smaller than zero indicate that participants did not respond as quickly as possible to go-signals—as it had been instructed—but instead awaited stop-signals in some of the go-trials. Therefore, data of 22 participants having negative SSRT-scores were excluded from further analysis.

Go/no-go task

The go/no-go task (adapted from [30, 79]) was written in Presentation (Neurobehavioral Systems). Following Rubia et al. [30] two experimental blocks were used. Each block included 150 trials (110 go- and 40 no-go-trials). In one block the go-stimulus was an arrow (11 cm width × 8 cm height) pointing to the right, in the other, it was an identical arrow pointing to the left. Participants were required to press a corresponding arrow key during both blocks with the index finger of their dominant hand. The no-go-stimulus was always an upward arrow, and participants were required not to respond at all when it appeared. The order of the two blocks was quasi-randomized across participants. Each trial involved a white arrow presented in the center of a black screen for 200 ms followed by a blank

screen lasting for 800 ms. The dependent variable was the percentage of commission errors, that is, errors on no-go-trials. Because of computer storage errors, go/no-go data from two participants were unavailable.

Eriksen flanker task

The task contained three conditions (neutral, congruent, incongruent). Participants were shown a white arrow (horizontal size approximately 5 cm, vertical size approximately 4 cm) which appeared in the centre of a black screen flanked on each side by two white squares (horizontal and vertical size approximately 5 cm) (neutral) or two other identical arrows pointing in the same (congruent) or opposite (incongruent) direction. Overall, the five stimuli were thus presented in a horizontal row. At the beginning of each trial, a central fixation cross was presented (horizontal size approximately 1.5 cm, vertical size approximately 1.5 cm) (500 ms), followed by the stimuli (1,000 ms) and all trials ended with a black screen (1,000 ms). The task comprised of 120 trials (40 of each condition, the number of right and left responses was balanced across conditions), presented in randomized order. The instruction emphasized to react only to the arrow in the middle by pressing the corresponding arrow key (right or left) on the keyboard. The dependent variable was the difference score of reaction times for incongruent and congruent condition.

Simon task

In the Simon task, participants are shown an arrow-like stimulus either in the right or in the left visual hemifield, and they are required to suppress the dominant tendency of responding congruently to the location of stimulus. Instead, they are required to only respond to the direction of the stimulus by pressing the corresponding arrow key (right or left). The task included two conditions, a congruent (stimulus direction matched stimulus location) and an incongruent condition (direction and location of stimuli were conflicting). In each trial, white triangles (horizontal size approximately 11 cm. vertical size approximately 9 cm) were presented for 400 ms on the left or right side of a dark screen followed by a cross (horizontal and vertical size approximately 1.5 cm) presented in the middle of the screen for 1,100 ms. Participants were shown 160 congruent to 60 incongruent trials in a random order. The dependent variables were the difference scores of incongruent and congruent condition's reaction times. 13 participants had accuracy rates lower than 40 % accuracy in the congruent or in the incongruent condition, which suggested they had misunderstood the task or had insufficient task motivation so they were not included in further analyses.

Statistical analysis

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) Release 15.0 (SPSS Inc., Chicago, IL, USA). First, outliers, cases with values falling at least two standard deviations below or above the mean, were detected and excluded. This procedure was applied to reaction time and interference score data of the Stroop, the Eriksen flanker and the Simon task, to the reaction time and error rate data of the go/no-go and the antisaccade task, and to the SSRT data. Second, as ADHD symptom checklists tend to show strongly right skewed distributions in non-clinical samples [80], we examined the distribution of scores on the ASRS and its subscales. Therefore, we created histograms and calculated skewness. Third, in order to explore the associations between demographic, psychometric and cognitive variables, Pearson's correlation coefficients were computed. Finally, hierarchical multiple linear regression analysis was conducted in order to test which inhibition-related measures can independently predict ADHD-like traits indicated by average scores on the ASRS and its subscales. In the first block age, gender, education, verbal intelligence and neuroticism were entered with the enter method in order to control for any possible confounding effect of these variables (see Online Resource 1 and [3, 4]). In the models, where one of the ASRS subscales was the dependent variable, the other ASRS subscale was also entered in the first block with the enter method. In the second block, antisaccade error rate, SSRT, go/no-go commission error rate, Stroop, Eriksen flanker and Simon task interference scores were entered with the stepwise method. Leave-one-out cross-validation (LOOCV) was performed, and mean squared errors (MSE) were compared with R (version 3.0.2) [81] to support model selection. LOOCV is a resampling method to estimate how well the model would fit new data collected in the corresponding population: greater MSE's indicate worse estimated fit.

Results

Distribution of ADHD-like traits

Histograms representing distributions of the total ASRS score and inattention and hyperactivity/impulsivity subscale scores of the ASRS are presented in Fig. 1. Histograms suggested largely normal distributions for these variables, supported by normal skewness values for the

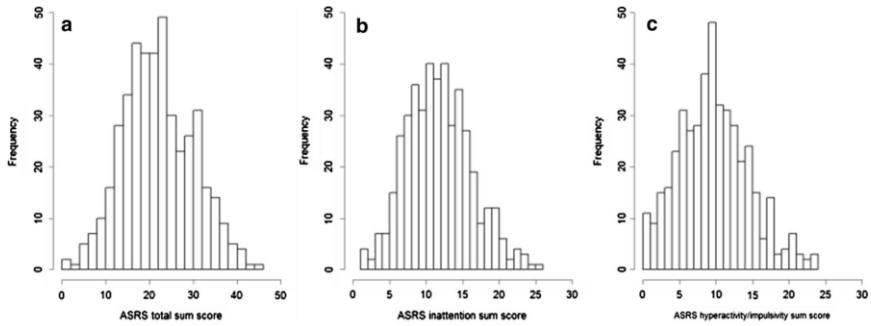

Fig. 1 Histograms representing the distributions of sum scores for the total ASRS (**a**), the inattention subscale (**b**) and the hyperactivity/impulsivity subscale (**c**)

total ASRS score (0.183) and the inattention (0.291) and hyperactivity/impulsivity subscales (0.295).

Correlations

The correlations between variables are presented in Online Resource 1. Age, verbal intelligence and education correlated weakly with some of the cognitive variables and ADHD-like traits. There was a moderate correlation between inattention and hyperactivity/impulsivity ($r = 0.55$, $p < 0.01$). Additionally, some correlations among different measures of inhibition-related functions were observed.

Linear regression models

The final model was significant for the overall ASRS score ($p < 0.001$, Table 2), yielding gender (higher score among males), neuroticism (entered in the first step) and Stroop interference score (entered in the second step) as significant predictors in the second step. The effect of go/no-go commission error rate was marginally significant ($p = 0.060$). LOOCV suggested slightly better performance of the model including Stroop interference score and go/no-go commission error rate ($MSE = 0.163$), relative to the model including only the control variables ($MSE = 0.166$).

Next, we wished to investigate how the inhibition-related variables might predict inattentive and hyperactive/impulsive traits separately (indicated by the two subscales of ASRS). The final model was significant for ASRS inattention, ($p < 0.001$, Table 3), yielding ASRS hyperactivity/impulsivity, gender (higher score among males) and neuroticism (entered in the first step) as significant predictors. The effect of Stroop interference score was marginally significant ($p = 0.068$). LOOCV suggested roughly equal performance of the model including only the control variables ($MSE = 0.163$) and the model additionally including Stroop interference score ($MSE = 0.163$). The final model for ASRS hyperactivity/impulsivity was significant as well ($p < 0.001$, Table 4), yielding ASRS inattention, neuroticism (entered in the first step) and go/no-go commission error rate (entered in the second step) as significant predictors. LOOCV suggested slightly better performance of the model additionally including go/no-go commission error rate ($MSE = 0.182$), relative to a model including only the control variables ($MSE = 0.183$).

Table 2 Summary of hierarchical multiple regression: predictors of the ASRS total mean score

Predictor	β	$t(434)$	p
First step			
Age	−0.07	−1.60	0.111
Gender	−0.09	−2.00	0.046
Education	−0.04	−0.92	0.356
MWT-B	−0.06	−1.33	0.183
Neuroticism	0.43	9.47	< 0.001
Second step			
Stroop interference	0.12	2.81	0.005
	2nd step R^2 change = 0.015		
Model statistics			
$R^2 = 0.207$, $R^2_{adj} = 0.196$	$F(6,434) = 18.59$		$p < 0.001$

Legend: *MWT-B*: Mehrfachwahl-Wortschatz-Intelligenztest, *ASRS* Adult ADHD Self-Report Scale. Gender: 1—male, 2—female. The following variables have been excluded from the final model: stop-signal reaction time; go/no-go commission errors; Eriksen flanker interference score; Simon task interference score; antisaccade error rate. Go/no-go commission error rate was marginally significant $\beta = 0.08$; $t(434) = 1.88$; $p = 0.060$

Table 3 Summary of hierarchical regression: predictors of the ASRS inattention subscale mean score

Predictor	β	$t(434)$	p
First step			
Age	−0.01	−0.19	0.847
Gender	−0.13	−3.03	0.003
Education	−0.01	−0.28	0.778
MWT-B	−0.01	−0.33	0.745
Neuroticism	0.28	6.42	<0.001
ASRS hyp/imp	0.46	11.16	<0.001
Model statistics			
$R^2 = 0.361$, $R^2_{adj} = 0.352$	$F(6,434) = 40.26$	$p < 0.001$	

Legend: *MWT-B* Mehrfachwahl-Wortschatz-Intelligenztest, *ASRS—hyp/imp* Adult ADHD Self-Report Scale, hyperactivity/impulsivity subscale. Gender: 1—male, 2—female. The following variables have been excluded from the final model: stop-signal reaction time; go/no-go commission errors; Eriksen flanker interference score; Simon task interference score; antisaccade error rate. Stroop interference was marginally significant $\beta = 0.07$; $t(434) = 1.83$; $p = 0.068$

Table 4 Summary of hierarchical regression: predictors of the ASRS hyperactivity/impulsivity subscale mean score

Predictor	β	$t(434)$	p
First step			
Age	−0.04	−0.84	0.400
Gender	0.04	0.81	0.420
Education	−0.03	−0.62	0.538
MWT-B	−0.05	−1.22	0.223
Neuroticism	0.11	2.45	0.015
ASRS inattention	0.48	11.10	<0.001
Second step			
Go/no-go %	0.10	2.37	0.018
	2nd step R^2 change = 0.009		
Model statistics			
$R^2 = 0.330$, $R^2_{adj} = 0.319$	$F(7,434) = 30.02$		$p < 0.001$

Legend: *MWT-B* Mehrfachwahl-Wortschatz-Intelligenztest; *ASRS* Adult ADHD Self-Report Scale, go/no-go %: go/no-go commission errors. Gender: 1—male, 2—female. The following variables have been excluded from the final model: stop-signal reaction time; Eriksen flanker interference; Simon task interference; Stroop interference; antisaccade error rate

Discussion

We found, after controlling for age, gender, education, verbal intelligence and neuroticism, that Stroop interference scores and, at trend level, go/no-go commission errors were positively associated with overall ADHD-like traits. Furthermore, go/no-go performance (predominantly reflecting motor inhibition) was specifically associated with hyperactivity/impulsivity, whereas Stroop performance (predominantly reflecting selective attention and interference control) tended to be associated specifically with inattention. Overall, these findings are in accordance with a meta-analysis indicating an association between Stroop performance and inattentive ADHD symptoms among patients with ADHD [35], while go/no-go performance has previously been linked to general ADHD-like traits in healthy children [62]. Additionally, brain activity related to response inhibition is correlated with inattentive and impulsive traits [63] among healthy participants. Overall, the trait-like "symptom" dimensions indicated by factor-analytical [55–60] and neurobiological [53, 82] approaches are nicely mirrored by the pattern of our results at the cognitive level.

Interpreting the Specific Relationships between ASRS and Measures of Inhibition

Intriguingly, out of the comprehensive test battery known to be sensitive to the inhibitory deficit usually reported in ADHD (e.g., [20, 24, 25, 30, 33]), only two tasks were related to ADHD-like traits in our sample of healthy adults. Therefore, we suggest that these two, namely Stroop and go/no-go, are not only potential endophenotypes of ADHD, as previous studies have suggested [37, 39, 40], but our results indicate that they are also sensitive to variation in ADHD-like traits in a population where these traits are only mildly expressed and who do not have any first-degree relatives with ADHD.

On the contrary, the antisaccade, the Simon, the Eriksen flanker and the stop-signal tasks were not related to ADHD-like traits in this sample. It is, therefore, possible that the impairments in ADHD observed in these paradigms [18–22, 24–28] only become apparent with the full biologic changes necessary for the expression of the clinical condition (e.g., [83] vs. [64]). It is additionally important to consider cognitive differences between the tasks. Despite conceptual similarities they each have unique requirements [7] which might be differently spared at the lower segment of the ADHD spectrum examined here. The lack of associations between ASRS scores and behavioral performance in the antisaccade, Simon, Eriksen flanker and stop-signal tasks may also be due to higher ASRS subjects' compensatory neural effort. Some studies showed no deficit of inhibition-related functions in ADHD in terms of behavioral performance but revealed differences in underlying neural activity [29, 84]. Future imaging studies are needed to clarify the neural aspects of individual differences in these tasks and their covariation with ADHD-like traits.

Considering the observation that response cancellation, as measured with the stop-signal task, shows an intermediate impairment in healthy first degree relatives of patients with ADHD [36–38], it is plausible that this deficit is more

proximal to familial risk factors. In contrast, as our sample included healthy people who did *not* have a first-degree relative with ADHD, the variation we observed in ADHD-like traits is probably less affected by the shared heritable factors of ADHD risk and response inhibition [45, 46]. Contrary to the literature on oculomotor abnormalities in ADHD, antisaccade error rate was not related to ADHD-like traits. The frequently reported higher antisaccade error rates in ADHD [25, 26, 28] may thus be a consequence of the expression of the full-blown clinical condition. Alternatively, these impairments may not be specific to the illness as they could be explained by more general emotional disturbances in one study [27].

The role of neuroticism and demographic factors

Neuroticism was the strongest predictor of ADHD-like traits in this study. Elevated levels of emotional instability are associated with categorical [85–88] and dimensional representations of ADHD [89], while the issue of causality between anxiety- and ADHD-related phenomena is controversial [90–92]. Nevertheless, the results suggest that affective disturbances might be important modulators of the heterogeneity of ADHD. Regarding demographic factors, only gender was related to ADHD-like traits. Males had higher scores on the ASRS (most driven by greater inattention), which is in line with gender differences observed in ADHD [3, 4].

Strengths and limitations

A notable strength of the study is that it examined a large, thoroughly screened sample of healthy adults, drawn not only from a university setting but also from the community. While the positive findings regarding the go/no-go and Stroop tasks are encouraging, the interpretation of null results concerning the other cognitive tasks is of course more problematic as non-significant correlations could indicate power problems or could be due to differential reliability of the tasks applied (regarding the stop task see [69, 93] and [23, 94–97]). Participants had no first-degree relatives with ADHD, which raises concerns about reducing variation in ADHD-like characteristics and undersampling healthy carriers of genes associated with elevated risk of ADHD, compared to other population-based studies [45, 62–66]. On the other hand, this sampling strategy enabled unconfounding individuals with high ADHD-like traits from unaffected relatives.

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Conflict of interest The authors declare that they have no conflict of interest.

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Research paper

Dopamine improves exploration after expectancy violations and induces psychotic-like experiences in patients with Parkinson's disease

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HIGHLIGHTS

- Exploration comprises the generation of new strategies and the search for patterns.
- Exploration and schizotypy were enhanced in groups of patients with Parkinson's.
- Dose-dependent effects of dopaminergic medications were observed.

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ABSTRACT

Dopamine neurons are sensitive to novel and rewarding events, and dopamine signals can modulate learning in higher-level brain networks. Additionally, dopamine abnormalities appear to be central to the pathophysiology of schizophrenia spectrum disorders. In this study, we investigate the dopaminergic modulation of schizotypal traits and exploration after expectancy violations in Parkinson's disease (PD) patients on dopamine replacement therapy. Exploration after expectancy violations was measured with a latent inhibition and an anomaly categorisation task. Patients with PD had significantly elevated levels of schizotypy and reduced latent inhibition, relative to the controls. Anomaly categorisation was enhanced at trend level among the patients. Dopaminergic antiparkinsonian drugs showed dose-dependent effects: they induced psychotic-like experiences, and at the same time, they disrupted latent inhibition and made categorisation of anomaly more efficient. Most of these findings were replicated in an independent sample of patients with PD. An up-regulated dopamine system in medicated PD patients might tune higher-level brain networks to engage in learning when faced with unexpected information, and therefore hasten the updating of internal models.

1. Introduction

It is a widely supported notion that organisms interact with the world via inferential processes involving the interplay of external stimulation and internal knowledge [1]. The brain constantly attempts to explain the causes of sensory data; predictions are matched with actual input, and prediction errors, reflecting the mismatch between expectation and experience, are propagated upwards in a hierarchy of representations to drive learning by updating internal models [2]. Distortions in this predictive system might lie at the core of distortion of reality in psychosis (i.e. hallucinations and delusions) [3,4], whose pathophysiology has been described in terms of a malfunctioning dopamine (DA) system [5].

In the healthy brain, DA neurotransmission signals various motivationally significant events, is involved in pursuing goals, and promotes learning in motivationally salient contexts [6]. Generally

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speaking, DA is assumed to drive behavioural and cognitive exploration, that is, actions and cognitions triggered by the 'incentive reward value of uncertainty' [7]. Cognitive exploration comprises the generation of new goals, strategies, and interpretations, and also the search for new patterns in perception and memory (see Ref. [7] for a thorough discussion). Rapid, phasic DA signalling is related to the processing of reward and novelty [8,9], while sustained, tonic DA signalling could potentiate learning and making effort under reward uncertainty [7,10].

DA replacement therapy is a widespread treatment of the motor symptoms of Parkinson's disease (PD) [11]. Antiparkinsonian drugs increase both tonic and phasic DA signalling [12,13]. In early phases of the disease, DA replacement therapy restores DA levels in brain areas where it is severely depleted (e.g. substantia nigra pars compacta, dorsal striatum), and overdoses DA in relatively unaffected areas (e.g. ventral tegmental area; VTA, ventral striatum; VS). Consequently, DA therapy can specifically improve and, at the same time, impair certain cognitive functions [14]. Psychotic-like experiences (hallucinations and delusions) can be present in PD with a lifetime prevalence above 50%, potentially stemming from complex interactions between pharmacological treatment and factors inherent to the disease itself [15,16].

Importantly, psychotic-like experiences are not limited to conditions of clinical relevance. Schizotypal traits represent subclinical individual variation in behavioural, emotional, and cognitive processes in the general population, which parallel the positive, negative, disorganised, and impulsive symptoms of schizophrenia [17–19]. A continuum between schizotypy in healthy people and schizophrenia is supported by accumulating evidence at multiple levels of analysis (for reviews see Ref. [19,20]). Crucially, abnormal dopaminergic neurotransmission seems to be involved not only in schizophrenia symptoms [5], but also in schizotypy (for a review see Ref. [17]). Interestingly, increased positive schizotypal traits have been documented in patients with PD undergoing dopaminergic therapy [21–23], which were correlated with aberrant attribution of salience to visual stimuli in one study [22].

The aim of the current research was to investigate the relationship between DA, schizotypy, and exploration after facing stimuli which violate expectations. Latent inhibition (LI) and false categorisation of anomaly could occur when behaviour is guided by previously learned, but actually incorrect predictions in unpredictable contexts. On the other hand, the lack of LI and successful categorisation of anomaly both could reflect the rapid updating of predictions when expectations are violated; more generally, they indicate exploratory behaviour in unpredictable situations.

LI refers to the common finding that repeated, nonreinforced presentation of stimuli can worsen performance in a later task where those stimuli become relevant, as compared to a task with novel targets [24]. LI stems from the maintained dominance of a formerly correct prediction ('those stimuli are unimportant') over behaviour in the later task, when that prediction turns erroneous [25,26]. Reduced LI has been documented in acute, but not chronic schizophrenia [24,25], and also in healthy participants high in positive schizotypy [27,28]. Crucially for the present study, DA agonists can disrupt LI in healthy humans [29,30]. Abnormalities of LI in unmedicated PD patients appear to be a function of gender and laterality of symptom onset [31]. However, to the best of our knowledge, so far no study has examined alterations of LI in PD patients undergoing dopaminergic treatment.

Bruner and Postman [32] demonstrated that people have difficulty in recognising an anomalous stimulus incongruent with their prior knowledge and expectations (a 'trick' playing card, with colour and suit reversed [e.g. three of hearts in black], presented amongst regular playing cards). In a later study, categorisation performance covaried with a measure of self-deception, suggesting that the tendency to accommodate experiences to expectations might have a trait-like component [33]. Additionally, efficient categorisation of anomaly in the cards experiment has been linked to better insight problem solving, implying that the ability to rapidly override expectations can benefit abandoning incorrect assumptions [34]. To date, however, no empirical study has investigated whether anomaly categorisation is linked to schizotypy or DA.

Given the conceptual relationship between LI and anomaly categorisation, and prior evidence linking DA, reduced LI, and schizotypy [17,27,29], we hypothesised that LI, anomaly categorisation, and positive schizotypy should be (a) interrelated and (b) altered in patients with PD undergoing dopaminergic treatment. Furthermore, we explored dose-dependent and medication-specific effects of DA among the patients, while controlling for demographic and disease-related factors.

Table 1
Demographic and clinical characteristics of the participants.

	PD	PD-R	Control
Age	55.2 (1.7)	56.2 (1.7)	56.7 (2.5)
Education (years)	12.3 (0.7)	12.7 (0.6)	12.2 (0.9)
IQ	110.5 (2.4)	107.8 (2.1)	108.3 (2.2)
Gender (M/F)	16/10	18/7	15/9
LED	657.5 (56.9)	752.8 (98.6)	–
UPDRS	35.5 (1.3)	44.1 (1.2)	–
Onset (left/right/NA)	8/17/1	17/8/0	–
Duration of illness (months)	12 (7; 48)	65 (20; 120)	–
Medication (Comb/L-DOPA/NO)	9/14/3	13/8/4	–

Data are means (standard errors), except for gender, onset, medication, and duration of illness. For duration of illness, medians (1st quartile; 3rd quartile) are reported. PD: Parkinson's disease, R: replication patient sample, IQ: general intelligence, LED: daily levodopa equivalent dose [34], UPDRS: Unified Parkinson's Disease Rating Scale score [35], NA: not available, NO: unmedicated, Comb: combined L-DOPA and dopamine agonist pharmacotherapy, L-DOPA: L-DOPA monotherapy.

2. Materials and methods

2.1. Participants

First, we recruited 26 non-demented patients with Parkinson's disease (PD) and 24 healthy controls matched for age, gender, education, and intelligence. These patients were recruited from a university clinic. Then, in order to improve the reliability of the study, we recruited an additional sample of 25 non-demented patients with PD (descriptive statistics are presented in Table 1). The second PD sample was recruited a year later, and these patients were from several outpatient centres in the city, including private ones. Age, education, intelligence, gender, and daily levodopa equivalent doses (LED [35]) of the two patient groups did not differ significantly (all p's > 0.39), while the differences in symptom severity (as indicated by the total Unified Parkinson's Disease Rating Scale (UPDRS) score [36]), disease duration and laterality were significant (all p's < 0.024). According to the clinical records and files of the patients, there was no evidence of impulse control disorders or dopamine dysregulation syndrome. This study was approved by the medical ethics committee and was conducted in accordance with the Declaration of Helsinki.

2.2. Procedures

Testing took place individually, in a quiet room. General intelligence was measured with the revised version of the Wechsler Adult Intelligence Scale [37]. Schizotypal traits were measured with the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE) questionnaire [18], which comprises four subscales: Unusual Experiences reflects hallucination- and delusion-like tendencies, Cognitive Disorganisation indicates loosened association and poor concentration, Introvertive Anhedonia measures reduced pleasure

and social withdrawal, and Impulsive Nonconformity taps asocial and impulsive behaviours.

Latent inhibition (LI) was measured with a visual search task, which is described in detail in Ref. [38]. The task consisted of two phases. In the preexposure phase trials, participants were requested to search for a target among distractors. The following test phase comprised two important conditions: the previous target became a distractor in both, and the target was either the previous distractor (preexposure condition) or a new stimulus (non-pre-exposure condition). The dependent variable reflecting LI was the difference between individual median reaction times obtained in the preexposure and the non-pre-exposure condition.

The card experiment described in Ref. [34] was used to examine categorisation of anomalous stimuli. In the present study, four normal playing cards were presented 12 times, while an anomalous 'trick' card (a black four of hearts) was presented 30 times. Participants were instructed to describe exactly what appeared on the screen, and the experimenter recorded responses as correct or incorrect (e.g. describing the anomalous card as 'a black four of hearts' vs. 'a four of spades'). The task began with a sequence including the randomised presentation of four normal playing cards, followed by the anomalous card. This sequence was repeated 12 times, and then only the anomalous card was shown 18 times. Stimulus duration progressively increased: the initial duration was 15 ms, which doubled after every third trial of a card (duration on the last trial was 7680 ms). The task was terminated upon the first correct categorisation of the anomalous card. The dependent variable was the number of presentations required for correct categorisation. If a participant could not identify the anomalous card correctly after 30 trials he received a score of 31. Data obtained in a pilot with undergraduates showed a distribution similar to that reported in Ref. [34].

2.3. Statistical analyses

We analysed the data with the statistical software R [39]. We first computed Spearman's rank correlation coefficients between schizotypy, LI, and anomaly categorisation in the first patient sample collapsed with the controls, and separately in the three groups as well. We corrected the correlations for multiple comparisons with Holm's method. Secondly, we compared the PD groups with the controls in terms of schizotypal traits, LI, and anomaly categorisation. If the Shapiro-Wilk test indicated non-Gaussian distribution, the Mann-Whitney test was applied; otherwise the two samples t-test was used. Thirdly, we investigated dose-dependent effects in the PD groups. To this end, we regressed dimensions of schizotypy, LI, and anomaly categorisation on LED scores. In order to control for demographic and disease-related factors, age, gender, symptom severity (total UPDRS scores), laterality of symptom onset, and duration of illness were also entered into each model. This protocol was performed separately for both patient samples. Finally, we collapsed the two patient samples for an exploratory analysis. We performed linear regressions to see whether the type of pharmacotherapy (levodopa monotherapy vs. combined) can predict schizotypy, LI, and anomaly categorisation over and above the effects of LED and the previously listed demographic and disease-related covariates.

3. Results

3.1. Covariation of schizotypy, latent inhibition, and anomaly categorisation

The correlations are presented in Table 2. Remarkably, several medium-to-strong correlations were observed between Unusual Experiences, LI, and anomaly categorisation. The pattern of relationships suggests that both tasks tap a process, which, in turn, is associated with positive schizotypy.

3.2. Comparing the PD and control groups

When we compared the patient samples to the controls, we found significantly higher levels of Cognitive Disorganisation ($t(48) = 4.52$, $p < 0.001$ and $t(47) = 3.23$, $p = 0.002$, for the comparison with the first and the replication PD sample, respectively) and significantly lower LI ($t(47) = -2.12$, $p = 0.039$ and $Z = -4.19$, $p < 0.001$, for the comparison with the first and the replication PD sample, respectively) in both PD groups. Unusual Experiences ($t(48) = 4.52$, $p < 0.001$) and Impulsive Nonconformity ($t(48) = 3.16$, $p = 0.003$) were significantly elevated in the first PD sample, and these patients also tended to correctly categorise the anomalous card after fewer trials ($Z = -1.76$, $p = 0.078$), relative to the controls. Introvertive Anhedonia was significantly higher in the replication PD sample ($t(47) = 2.83$, $p = 0.007$), relative to the controls. No other differences between the patient samples and the controls were significant (all p values > 0.18). Descriptive statistics and effect sizes are reported in Table 3. Recognition performance for normal playing cards was high and did not differ significantly between groups (median correctly recognised normal cards: 97%, 89%, and 80% and for controls, the first, and the replication PD sample, respectively, all p values > 0.15).

3.3. Dose-dependent effects of dopaminergic medications in PD

The relationships between LED, schizotypy, LI, and anomaly categorisation in the first sample of patients are shown in Fig. 1. In the first patient sample, Unusual Experiences were significantly and positively predicted by LED ($\beta = 0.52$; $t = 2.94$; $p = 0.009$; $F(6.18) = 3.04$; $R^2_{adj} = 0.34$; $p = 0.031$; all p values of covariates > 0.25). Cognitive Disorganisation was also significantly and positively predicted by LED ($\beta = 0.50$; $t = 2.76$; $p = 0.012$; $F(6.18) = 2.65$; $R^2_{adj} = 0.29$; $p = 0.051$; the effect of age was significant: $\beta = 0.55$, $t = 2.33$; $p = 0.032$, p values of all the other covariates > 0.16). Neither Introvertive Anhedonia nor Impulsive Nonconformity were significantly associated with the predictors (all F values <1.26 and all p values >0.32). LI was significantly and negatively predicted by LED ($\beta = -0.68$; $t = -3.89$; $p = 0.001$; $F(6.18) = 3.15$; $R^2_{adj} = 0.35$; $p = 0.027$; all p values of covariates >0.43), suggesting a dose-dependent disruptive effect of dopaminergic drugs on LI. Finally, anomaly categorisation performance was also significantly and negatively predicted by LED ($\beta = -0.72$; $t = -4.12$; $p < 0.001$; $F(6.18) = 3.05$; $R^2_{adj} = 0.34$; $p = 0.031$; right onset of symptoms had a marginally significant negative effect, $\beta = -0.35$; $t = -1.77$; $p = 0.095$, p values of all the other covariates >0.45).

In the replication sample, Unusual Experiences ($\beta = 0.70$; $t = 3.13$; $p = 0.006$; $F(6,18) = 3.35$; $R^2_{adj} = 0.37$; $p = 0.021$, all p values of covariates > 0.14) and Cognitive Disorganisation ($\beta = 0.70$; $t = 3.39$; $p = 0.003$; $F(6,18) = 4.50$; $R^2_{adj} = 0.47$; $p = 0.006$; all p values of covariates >0.31) were positively and significantly predicted by LED, while neither Introvertive Anhedonia or Impulsive Nonconformity were significantly associated with the predictors (all F values <0.68 and all p values >0.67). Again, LI was significantly and negatively predicted by LED ($\beta = -0.45$; $t = -2.30$; $p = 0.033$; $F(6,18) = 5.60$; $R^2_{adj} = 0.53$; $p = 0.002$; age had a significant effect: $\beta = 0.75$; $t = 3.59$; $p = 0.002$, p values of all the other covariates > 0.13). The model predicting anomaly categorisation was almost significant ($F(6,18) = 2.66$; $R^2_{adj} = 0.29$; $p = 0.050$). In this model, LED ($\beta = -0.74$; $t = -3.12$; $p = 0.006$) and PD symptom severity ($\beta = -0.52$; $t = -2.19$; $p = 0.042$) had significant negative effects (p values of all the other covariates > 0.19).

Table 2
Spearman's rho rank correlations between schizotypy, latent inhibition, and anomaly categorisation in the first PD/replication PD/control group.

	CD	IA	IN	LI	AC
UE	0.16/***0.61***/***0.78***	−0.09/0.15/0.05	−0.18/**0.52**/***0.66***	***−0.44***/***−0.56***/***−0.68***	−0.31/***−0.61***/***−0.69***
CD		−0.35/0.17/0.25	−0.10/**0.63**/***0.72***	−0.01/***−0.42***/***−0.47***	−0.17/***−0.45***/***−0.53***
IA			0.05/−0.22/−0.03	0.00/−0.22/0.04	−0.04/−0.05/−0.07
IN				0.34/−0.20/−0.34	0.21/−0.39/−0.27
LI					***0.70***/***0.65***/***0.55***

UE: Unusual Experiences, CD: Cognitive Disorganisation, IA: Introvertive Anhedonia, IN: Impulsive Nonconformity, LI: latent inhibition, AC: anomaly categorisation. Significant correlations ($p < 0.05$, uncorrected) are highlighted in **bold**. Correlations surviving Holm's correction method are additionally highlighted in ***italics***.

When we collapsed the two patient samples, we found that patients on levodopa monotherapy exhibited significantly higher Cognitive Disorganisation ($\beta = 0.29$; $t = 2.06$; $p = 0.047$) and greater LI ($\beta = 0.38$; $t = 2.81$; $p = 0.008$), compared to patients receiving combined (levodopa and DA agonist) pharmacotherapy. Medication type did not have a significant impact on other dimensions of schizotypy or anomaly categorisation (all p values >0.46). Importantly, these effects were observed over and above the effect of LED, demographic, and clinical covariates. The pattern of associations between LED and the dependent variables was essentially unchanged in the collapsed patient sample, relative to what was found in the separate patient groups.

4. Discussion

In this study, we provided evidence, for the first time, that the DA systems are involved in anomaly categorisation. Our findings have also confirmed previously established links between DA, LI, and positive schizotypy [17,27,29]. Furthermore, we demonstrated that categorisation of anomaly is associated with reduced LI and positive schizotypy. Despite clinical heterogeneity, the association between LED and positive schizotypy, LI and anomaly categorisation were replicated in an independent sample of patients. On the other hand, impulsive and positive schizotypy, and anomaly categorisation were elevated only in the first PD group, while negative schizotypy was elevated only in the replication PD group, as compared to healthy controls. The majority of the first patient sample had early PD (duration <5 years), while the replication group comprised relatively more patients with late PD (duration >5 years, see Table 1). This might bear relevance as medication can differently affect cognitive functions in more progressed PD [40]. The regression analyses suggested that age, PD symptom severity, and laterality of symptom onset might be related to some of the inconsistencies found in this study.

Globally, our results match the idea that DA is a key neurotransmitter underlying behavioural and cognitive exploration [7]. In the healthy brain, DA signals code reward, novelty [8,9], and uncertainty [10], and promote learning and approach in salient contexts [6,7]. Illustrating DA's role in exploration, activation in the human dopaminergic midbrain (i.e., the VTA) during anticipation of novelty or reward has been shown to predict improvement of exploration-related hippocampal functions, such as processing of novel [8] and unexpected information [41]. In early PD, however, DA therapy could upregulate signalling in the relatively unaffected VTA, VS, and related structures [14]. In turn, the elevated DA activation in these regions might modulate a cortico-hippocampal network to obtain enriched information from the environment without regard to the salience of the context [41], possibly biasing cognition towards exploration.

Supporting this idea, levodopa has been found to diminish neural discrimination between novel and familiar images in the VTA of healthy adults (i.e.the VTA responded to familiar information as if it was novel), and greater reduction in such discrimination predicted better memory for the encountered information [42]. Interestingly, a recent study found that patients with PD on DA replacement treatment had disproportionally enhanced recognition memory for irrelevant background scenes in a visual detection task, irrespective of motivational context [43]; probably explicable by augmented communication between the VTA and the hippocampus. It is noteworthy that dopaminergic medications in PD have been reported to induce behavioural changes associated with exploration, such as increased novelty seeking [44] or enhanced creative thinking [45].

We propose that hyperassociative learning and the consequent tendency to perceive unlikely patterns could be a commonality between reduced LI and successful anomaly categorisation [7,26]. On one hand, easily changeable predictions can be adaptive and contribute to insight problem solving [34] and creativity [38]. On the other hand, an excess tendency to perceive implausible patterns [7] can be maladaptive; recent accounts of psychosis emphasise that symptoms of reality distortion arise due to abnormal predictive mechanisms [3] and aberrant salience [5]. For instance, neural correlates of impaired distinction between motivationally salient (rewarding or aversive) and neutral events covaried with delusional pathology in patients with schizophrenia [46,47].

A study reported elevated positive and disorganised schizotypy in patients with PD, who were receiving dopaminergic treatment, and had no impulse control disorders (ICD). Patients with ICDs additionally demonstrated elevated negative and impulsive schizotypy, relative to healthy controls. When all patients with PD were combined with the controls, explicit and implicit measures of aberrant salience correlated with negative and disorganised schizotypy, respectively. Furthermore, LED correlated positively with impulsive schizotypy [21]. Another study longitudinally examined patients with PD receiving DA agonists. Relative to the unmedicated baseline, adaptive and aberrant salience were elevated, together with increased positive schizotypy. In the medicated state, aber-

Table 3
Means (standard errors) of schizotypy dimensions, latent inhibition, and anomaly categorisation in the sample.

	PD	PD − R	Control	Effect size (PD vs. control)	Effect size (PD − R vs. control)
Unusual Experiences	12.12 (0.6)	9.24 (0.6)	8.08 (0.6)	1.28	0.38
Cognitive Disorganisation	10.12 (0.9)	9.12 (0.6)	6.54 (0.5)	0.97	0.92
Introvertive Anhedonia	4.62 (0.6)	8.64 (0.8)	5.75 (0.6)	0.38	0.80
Impulsive Nonconformity	10.85 (1.0)	8.48 (0.9)	6.83 (0.8)	0.89	0.39
Latent inhibition	0.18 (0.1)	0.04 (0.0)	0.34 (0.0)	0.61	1.32
Anomaly categorisation	2 (1; 3.75)	9 (2; 27)	4.5 (2; 14.25)	0.28	0.12

Cohen's d is provided as an indicator of effect size. R indicates the replication sample. In the case of anomaly categorisation, medians (1st quartile; 3rd quartile) and Cliff's Delta effect sizes are reported.

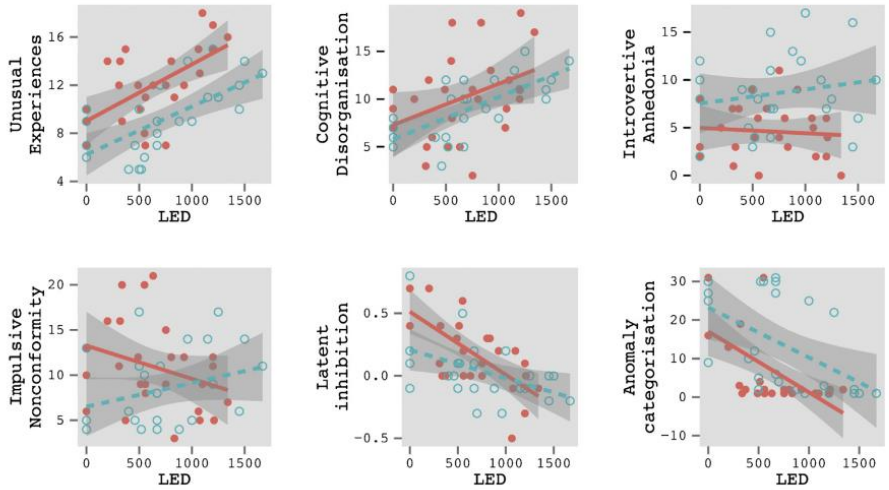

Fig. 1. Levodopa equivalent doses of patients with PD plotted against dimensions of schizotypy, latent inhibition, and anomaly categorisation. The first PD sample is plotted with filled circles and a continuous trend line (red in online), while the replication PD sample is plotted with hollow circles and a dashed trend line (blue in online). Dark grey shadings indicate 95% confidence intervals (see Section 3.3 for details).

rant salience correlated with positive schizotypy [22]. In a different longitudinal study, positive schizotypy was elevated in PD patients taking DA agonists, relative to unmedicated baseline. Moreover, baseline schizotypy scores predicted DA agonist-induced changes in divergent thinking, an indicator of creative potential [23]. The present findings suggest that beyond aberrant salience, reduced latent inhibition (and perhaps enhanced anomaly processing) could contribute to DA-related schizotypy in PD.

The low sample size limits generalisation of the findings of our study. Additionally, although dose-dependent effects of DA drugs were present when the analyses were controlled for main demographic and disease-related factors, there might be other sources of differences specific to PD itself. Therefore the present findings must be cautiously extrapolated to DA function in the healthy human brain. In this regard, a replication with healthy participants and similar DA agents would be valuable. It also should be noted that altered salience processing in PD might involve neurotransmitters other than DA [48]. Our exploratory analyses suggested that levodopa monotherapy might affect disorganised schizotypy more and LI less, as compared to a combined levodopa – DA agonist therapy. However, as patients were on mixed therapies, we were unable to precisely differentiate the effects of levodopa and DA agonists on cognition and schizotypy (for a computational framework see Ref. [49]). DA agonists have been reported to increase the risk of ICDs in PD [50]. Although the clinical records and files of the patients indicated no evidence of ICDs or dopamine dysregulation syndrome, DA agonist-induced subtle ICD-like effects might confound the results.

Competing interests

None.

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Study related to thesis point 4

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Kiss of the Muse for the Chosen Ones: De Novo Schizotypal Traits and Lifetime Creative Achievement Are Related to Changes in Divergent Thinking During Dopaminergic Therapy in Parkinson's Disease

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Creativity can arise in some Parkinson's disease (PD) patients as a side effect of dopaminergic therapy. Schizotypal traits—subclinical traits resembling schizophrenia symptoms—can mediate some effects of dopaminergic drugs on cognition and neural activity. The goal of our study was to relate general intelligence, creative achievement and schizotypal traits to changes in performance on the Just Suppose test (from the Torrance battery), a task designed to measure verbal divergent thinking. Patients with PD and controls were examined at baseline, and at a follow-up session 12 weeks after pharmacotherapy had begun. Patients received dopamine agonist monotherapy (pramipexole and ropinirole). We observed significantly elevated positive schizotypy and impulsivity in PD at follow-up, while divergent thinking scores increased at trend level in the patient group. Linear regression analyses revealed that changes in various aspects of divergent thinking in PD were related to positive and disorganized schizotypy and lifetime creative achievement. The results highlight the relevance of schizotypal traits and lifetime creative achievement to the development of creativity in PD during dopaminergic therapy. The research draws attention to individual differences associated with a side effect of dopaminergic therapy in PD and also contributes to the understanding of the biological aspects of creativity.

Keywords: Parkinson's disease, dopamine, pharmacotherapy, divergent thinking, schizotypy

Studies of patients with neurological conditions can provide valuable insights into the neural aspects of cognitive processes related to creativity and art (e.g., Abraham, Beudt, Ott, & Yves von Cramon, 2012; Maurer & Prvulovic, 2004; Miller et al., 1998; Shamay-Tsoory, Adler, Aharon-Peretz, Perry, & Mayseless, 2011; van Buren, Bromberger, Potts, Miller, & Chatterjee, 2013). Parkinson's disease (PD) is characterized by salient motor symptoms and various additional nonmotor disturbances (see Chaudhuri & Schapira, 2009; Hawkes, Del Tredici, & Braak, 2010, for reviews). The disease shows a progressive multistage course with the onset of main motor symptoms only at intermediate stages, when neurodegenerative processes extend to dopaminergic structures in the midbrain (Braak et al., 2003). Dopamine receptor agonist pharmacotherapy is a well-established treatment for remediating the motor symptoms of PD (Parkinson Study Group, 2000).

Possible *side effects of the treatment* include impulse control disorders (ICDs, pathological gambling, compulsive sexual, buying and eating behavior), dopamine dysregulation syndrome (excessive self-administration of dopaminergic drugs), and other impulsive–compulsive behaviors (punding [repetitive, stereotyped behaviors without any goal], hobbyism, walkabout [immoderate, purposeless wandering], and hoarding; Weintraub & Nirenberg, 2013). Furthermore, some medicated patients report psychotic experiences like hallucinations and delusions (Fénelon & Alves, 2010).

It has been suggested that dopaminergic therapy is associated with increased creativity, as a somewhat more delightful "side effect." Emerging creativity as a consequence of dopaminergic therapy has been documented in the domain of visual arts (Canesi, Rusconi, Isaias, & Pezzoli, 2012; Chatterjee, Hamilton, & Amora-

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panth, 2006; Kulisevsky, Pagonabarraga, & Martinez-Corral, 2009; López-Pousa et al., 2012; Walker, Warwick, & Cercy, 2006), poetry (Canesi et al., 2012; Joutsa, Martikainen, & Kaasinen, 2012; Schrag & Trimble, 2001), and sculpting (Canesi et al., 2012). A study examining a group of patients with PD has shown that those patients, who started to produce various forms of art after dopaminergic treatment, reached a higher score on a composite assessment of *divergent thinking*, compared to patients who had not developed such artistic tendencies (Canesi et al., 2012). Another systematic study found reduced performance in terms of fluency and total scores on a verbal divergent thinking task only in PD patients with right hemibody onset, compared to matched controls and patients with left hemibody onset (Drago, Foster, Skidmore, & Heilman, 2009). However, it is still under debate whether a direct relationship would occur between pharmacotherapy and creativity and how other psychological effects (e.g., impulsivity, elevated mood, psychotic-like experiences) might mediate this relationship (Canesi et al., 2012; Joutsa et al., 2012). It has recently been proposed that dopamine dysregulation syndrome in PD might be associated with creative professions (Schwingenschuh, Katschnig, Saurugg, Ott, & Bhatia, 2010), but the relevance of creative occupation and achievement to developing creativity in PD has not been tested so far. Interestingly, reports of augmented creativity are limited to a subset of PD patients (Canesi et al., 2012) and our understanding of individual differences in the "creativity side effect" is just developing (Drago et al., 2009).

Creativity is a highly complex phenomenon requiring a comprehensive definition. According to Plucker, Beghetto, & Dow (2004), it is best viewed as "the interaction among *aptitude, process, and environment* by which an individual or group produces a *perceptible product* that is both *novel and useful* as defined within a *social context*" (p. 90, emphasis in original). Amabile (1983) identified intrinsic motivation, domain-relevant and creativity-relevant skills as components essential to creativity. Divergent thinking, as a creativity-relevant skill, is assumed to exert its greatest influence in the response generation or ideation phase of the creative process (Amabile, 1983; Brophy, 1998). Although divergent thinking is necessary for real life creative achievements, in itself it seems insufficient (Batey & Furnham, 2006). Divergent thinking test scores offer a fairly reliable estimate of creative potential (Plucker, 1999; Plucker & Makel, 2010; Runco, 2010; Runco & Acar, 2012). The investigation of divergent thinking in patients with PD undergoing dopaminergic treatment provides a unique opportunity to compound psychometric and biometric methodologies in creativity research (Plucker & Renzulli, 1999).

Data from genetic (Mayseless, Uzefovsky, Shalev, Ebstein, & Shamay-Tsoory, 2013; Murphy, Runco, Acar, & Reiter-Palmon, 2013; Reuter, Roth, Holve, & Hennig, 2006; Runco et al., 2011) and neuroimaging (de Manzano, Cervenka, Karabanov, Farde, & Ullén, 2010; Takeuchi et al., 2010) studies demonstrated the role of dopaminergic systems in divergent thinking. The neurotransmitter dopamine plays fundamental roles in various functions in the central nervous system and in the periphery as well (Beaulieu & Gainetdinov, 2011). Particularly intriguingly for the present study, its relevance has been documented with respect to learning (Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006), motivation (Depue & Collins, 1999), risk taking, and attention (Fiorillo, Tobler, & Schultz, 2003). Dopaminergic systems in the brain are involved in neural processes representing reward, salience (Smith, Li, Becker, & Kapur, 2006), and uncertainty (Fiorillo et al., 2003). Latent inhibition (Carson, Peterson, & Higgins, 2003; Kéri, 2011) and reward sensitivity (Bódi et al., 2009; Heilman, Nadeau, & Beversdorf, 2003) are possible links between dopamine and creativity at the level of basic cognitive processes.

Dopamine's action on physiology is mediated by five subtypes of receptors, which can be classified into the D1 (D1 and D5 receptor subtypes) or the D2 (D2, D3, and D4 subtypes) families (Beaulieu & Gainetdinov, 2011). Dopamine receptor agonists mimic the action of endogenous dopamine on these receptors and they differ in their selectivity for particular receptor subtypes. Both of the dopamine agonists investigated in the present study, namely pramipexole and ropinirole, can be regarded as selective D2 receptor agonists, and pramipexole additionally shows high selectivity for the D3 subtype (Beaulieu & Gainetdinov, 2011; Gerlach et al., 2003). D2 and D3 receptors are mostly expressed in the striatum, the limbic areas, and, to a limited extent, in the substantia nigra, the ventral tegmental area, and in some cortical areas as well (Beaulieu & Gainetdinov, 2011).

Due to the spatiotemporal course of progression of PD, it has been suggested that dopaminergic therapy has contrasting effects on distinct loops of the frontostriatal dopaminergic systems (Cools, 2006). Dopaminergic drugs are thought to restore dopamine levels in the dorsal frontostriatal loop, which is damaged at earlier stages of the disease. At the same time, dopaminergic pharmacotherapy could overdose the ventral frontostriatal loop, which gets affected only later in the disease course. Therefore, dopaminergic treatment in PD can remediate some and at the same time disrupt certain other cognitive functions (Cools, 2006; Cools & D'Esposito, 2011).

Studies involving healthy individuals indicated that *schizotypal traits*—personality traits resembling positive, negative and disorganized symptoms of schizophrenia in a subclinical fashion (Ettinger, Meyhöfer, Steffens, Wagner, & Koutsouleris, 2014; Mason & Claridge, 2006)—mediate some effects of dopaminergic drugs on cognition (Kumari et al., 1999; Mohr, Krummenacher, et al., 2005; Mohr, Landis, Bracha, Fathi, & Brugger, 2005; Schmechtig et al., 2013). Several genetic studies implicated correlations between schizotypal traits and the variants of the catechol-O-methyltransferase (COMT) gene, which indirectly cause reduced dopamine neurotransmission in the prefrontal cortex (Avramopoulos et al., 2002; Grant et al., 2013; Schürhoff et al., 2007; Smyrnis et al., 2007; Stefanis et al., 2004). On the other hand, there have been somewhat less conclusive findings too (Ma et al., 2007; Sheldrick et al., 2008), which might be explicable by epigenetic effects in action (Alemany et al., 2014; Savitz, van der Merwe, Newman, Stein, & Ramesar, 2010). Imaging studies showed association of schizotypal traits and striatal and extrastriatal dopamine release induced either by d-amphetamine (Woodward et al., 2011) or stress (Soliman et al., 2008), and schizotypal traits have also been linked to the degree of stress-induced striatal and limbic activity changes (Soliman et al., 2011). In a previous study, we found that dopamine agonist therapy increased positive schizotypal traits in PD, together with an abnormal attribution of salience to visual stimuli (Nagy et al., 2012). However, it has not been clarified whether these changes in personality and cognition would be associated with enhanced creative potential.

To the best of our knowledge, no study has so far examined the role of schizotypal traits in modulating the effect of dopaminergic drugs on divergent thinking, a putative correlate of creativity (Heilman et al., 2003; Runco & Acar, 2012). In light of the aforementioned findings, we hypothesized that individual differences in schizotypy would correlate with changes in divergent thinking during dopamine agonist therapy in PD. In addition to divergent thinking, which is a laboratory-based correlate of creativity (Carson et al., 2003; Carson, Peterson, & Higgins, 2005; Jauk, Benedek, Dunst, & Neubauer, 2013), we also assessed real-life creative achievements. We predicted that general intelligence and lifetime creative achievement would be associated with changes in divergent thinking in PD (Kell, Lubinski, Benbow, & Steiger, 2013). Finally, as verbal fluency and divergent thinking have recently been suggested to be strongly intertwined (Silvia, Beaty, & Nusbaum, 2013), we measured letter fluency to see whether a rather general enhancement of broad retrieval ability could explain any improvement in divergent thinking.

Method

Participants

We recruited 18 newly diagnosed, previously unmedicated patients with PD. The diagnosis was established according to the U.K. Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria (Hughes, Daniel, Kilford, & Lees, 1992). The symptoms of PD were evaluated with the Unified Parkinson's Disease Rating Scale (Lang & Fahn, 1989). Seven patients had left and 11 patients had right hemibody symptom onset. The PD patients were compared with 19 matched healthy volunteers. After baseline testing in unmedicated state, patients received dopamine agonist monotherapy and were followed-up for 12 weeks when they were reevaluated (pramipexole: $n = 10$, mean dose at follow-up: 4.5 mg/day, range: 2.5–6.0 mg/day; ropinirole: $n = 8$, mean dose at follow-up: 9.0 mg/day, range: 5.0–11.5 mg/day). We also assessed the control volunteers two times to check the reliability of assessment. All scales, including clinical and neuropsychological assessments, were administered by trained experts who were blind to diagnosis, test performance, medication status, and the aims of the study. All participants gave written informed consent and the study was approved by the institutional ethics board. The demographic data are summarized in Table 1.

Table 1
Descriptive Statistics of the Sample

	Controls	PD
N	19	18
Age (years)	48.0 (7.2)	47.6 (7.7)
Education (years)	11.6 (3.3)	11.8 (3.8)
Gender (male/female)	12/7	11/7
IQ	107.8 (9.8)	106.2 (14.0)
Creative achievement (CAQ)	5.4 (6.2)	4.4 (5.6)

Note. PD = Parkinson's disease; IQ = intelligence measured with the Wechsler Adult Intelligence Scale; CAQ = Creative Achievement Questionnaire. Data indicate means, with standard deviations in parentheses. IQ and creative achievement were measured only at baseline.

General Cognitive Functions and Verbal Fluency

General intellectual functions were measured at baseline using the revised version of the Wechsler Adult Intelligence Scale (Wechsler, 1981). We assessed letter fluency with the F-A-S test at baseline and at follow-up as well (Spreen & Benton, 1977). Participants were requested to orally produce as many words as possible that began with the letters F, A, and S within 1 min. The dependent measure was the total number of words recalled.

Divergent Thinking and Real-Life Creative Achievements

We used the Just Suppose subtest of the Torrance Test of Creative Thinking (Torrance, 1974) to examine divergent thinking in the verbal domain. Test items from the two different forms were used at baseline and at follow-up. An example is when participants were asked, "Just suppose clouds had strings attached to them which hang down to earth. What would happen? List your ideas and guesses." In the instructions, we emphasized that participants should try to come up with original, creative ideas and also should give as many answers as they can. Responses are scored for originality, flexibility, and fluency. The originality score reflects the statistical infrequency of each individual response within the current sample. The flexibility score reflects changes in focus during in the associations and is scored through the number of shifts between categories. Finally, the fluency score is based on the number of different possibilities produced. The Just Suppose test was scored following the instructions provided in the manual (Torrance, 1974), by two trained experts, who were blind to study aims. Interrater consistency was high (intraclass correlation $r > .8$).

Lifetime creative achievements were evaluated with the Creative Achievement Questionnaire (CAQ) at baseline (Carson et al., 2005). Participants rated achievements in 10 domains of creative accomplishment (visual arts, music, dance, architectural design, creative writing, humor, inventions, scientific discovery, theater and film, and culinary arts). For example, in the visual arts domain the participant was asked to mark the statement that best described his or her achievements (e.g., "People have commented on my talent in this area," "I have won a prize or prizes at a juried art show," "My work has been critiqued in national publications"). The total CAQ score is the sum of the weighted scores from the 10 domains (Carson et al., 2005). The CAQ domain scores showed good reliability in this sample (Cronbach's alpha 0.77−0.85), although traditional reliability analysis is problematic in the case of the CAQ (see Silvia, Wigert, Reiter-Palmon, & Kaufman, 2012).

Schizotypy and Impulsivity

Schizotypy and impulsivity were measured at baseline and at follow-up. The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason, Claridge, & Jackson, 1995) questionnaire was used to assess everyday versions of feelings and experiences related to psychotic states. The O-LIFE consists of 159 items in a yes/no response format. Items are classified into four dimensions: Unusual Experiences (perceptual aberrations, magical thinking, and hallucinatory experiences), Introvertive Anhedonia

(decreased pleasure and enjoyment from social and physical sources of pleasure and the avoidance of intimacy), Cognitive Disorganization (loosened association and poor concentration), and Impulsive Nonconformity (impulsive, eccentric, aggressive, and asocial traits). All dimensions of the O-LIFE showed good reliability in this sample (Cronbach's alpha values 0.80, 0.77, 0.76 and 0.72, for Unusual Experiences, Introvertive Anhedonia, Cognitive Disorganization, and Impulsive Nonconformity, respectively). Given that impulsivity is a common side effect of dopamine agonist therapy, we also administered the Barratt Impulsiveness Scale (BIS-11), evaluating three dimensions of impulsivity (motor impulsivity, attentional impulsivity, and nonplanning; Patton, Stanford, & Barratt, 1995). The BIS-11 had good reliability in this study (Cronbach's alpha = .82).

Statistical Analysis

Exploratory analyses. Statistical analyses were performed with SPSS Release 15.0 and with the statistical software R 3.0.2 (R Core Team, 2014). Shapiro-Wilk tests were applied to test for normality of distribution. When the data showed non-Gaussian distribution, we applied transformations to normalize the distribution where it had been possible, otherwise we used nonparametric tests. We conducted independent sample *t* tests and Mann–Whitney *U* tests to compare the two groups' age, IQ, education, lifetime creative achievements (CAQ), trait impulsivity (BIS) and schizotypy (O-LIFE), divergent thinking (Just Suppose), and letter fluency (F-A-S) performance at baseline. We calculated Spearman's rho rank correlation coefficients to explore relationships between measures at baseline and at follow-up, separately for the two groups.

Between-session changes. First, in order to explore between-session changes, two-factor design (Group: PD vs. Controls × Session: Baseline vs. Follow-Up) repeated-measures analyses of variance (ANOVAs) were performed for the variables measured both at baseline and at follow-up. These were the dimensions of schizotypy indicated by the O-LIFE subscales, trait impulsivity indicated by the BIS-11, aspects of divergent thinking indicated by the subscores of the Just Suppose test, and letter fluency indicated by the F-A-S test. When the Group × Session interaction was significant, post hoc analyses were carried out by means of linearly independent pairwise comparisons, with Bonferroni adjustment for multiple comparisons.

Individual differences in between-session changes. In order to examine individual variation in between-session change of divergent thinking scores, hierarchical multiple regressions were conducted. Based on previous results, we identified general intelligence (as reflected by the Wechsler Adult Intelligence Scale score; Carson et al., 2003; Kell et al., 2013; Kéri, 2011), lifetime creative achievements (as reflected by the CAQ score; Schwingenschuh et al., 2010) and dimensions of schizotypy (as reflected by the O-LIFE subscale scores; Kumari et al., 1999; Mohr, Krummenacher, et al., 2005, Mohr, Landis, et al. 2005; Schmechtig et al., 2013; Soliman et al., 2008, 2011; Woodward et al., 2011) as potential baseline predictors of individual differences in change of divergent thinking during dopamine agonist treatment.

Originality, fluency, and flexibility scores obtained at follow-up served as dependent variables. The independent variables were entered in three blocks. In the first block, the baseline originality, fluency, or flexibility score was entered to control for pretreatment differences in divergent thinking. Considering that the sample size did allow entering only a few predictors into a model, we tested the effect of each baseline predictor in separate series of steps. In the second block, one of the above listed a priori selected baseline predictor variables and a dummy variable coding group membership (PD = 1) were entered. Finally, in the third block, the interaction between the baseline predictor variable and group membership were entered.

Note that the effect of a baseline divergent thinking variable indicates the shared variance between baseline and follow-up divergent thinking scores in the whole sample. In the second step, the effect of the grouping variable indicates between-groups differences in divergent thinking at follow-up, while the baseline divergent thinking and a baseline predictor are controlled. The effect of the baseline predictor variable in the second step indicates its relationship to between-session change in divergent thinking throughout the whole sample. In the third step, the baseline predictor's effect on between-session change in divergent thinking is evaluated separately in PD and among controls with the interaction term and with the single term, respectively.

Results

Exploratory Analyses

Descriptive statistics are presented in Table 1 and 2. Patients and controls did not differ in terms of any of the variables at baseline (all $ps > 0.42$, independent-sample *t* tests and Mann–Whitney *U* tests). Correlations between all measures at baseline and at follow-up in the PD and in the control group are presented in Table 3 and 4, respectively.

Between-Session Changes

Acceptable distributions were achieved after logarithmic transformation of the divergent thinking subscores (all Shapiro-Wilk tests' $p > .046$). In the PD group, we observed a significant decrease in Parkinsonian symptoms (mean Unified Parkinson's Disease Rating Scale scores and standard deviation in parentheses, baseline: 35.8 (10.3), follow-up: 24.2 (9.6), paired-samples *t* test $p < .05$), indicating clinical improvement.

The main effect of session (baseline vs. follow-up) in the repeated-measures ANOVAs was significant for the Unusual Experiences score, $F(1, 35) = 22.17$, $p < .001$, the Impulsive Nonconformity score, $F(1, 35) = 5.98$, $p = .020$, for trait impulsivity (BIS-11 score), $F(1, 35) = 9.39$, $p = .004$, for the fluency, $F(1, 35) = 10.95$, $p = .002$, and the flexibility score, $F(1, 35) = 14.46$, $p = .001$, suggesting significant changes from baseline to follow-up, when data were collapsed across groups. The main effect of session was not significant for the Introvertive Anhedonia score, the Cognitive Disorganization score, the originality score and the F-A-S test score (all $ps > 0.61$ and all $Fs < 0.26$), suggesting no significant changes from baseline to follow-up, when data were collapsed across groups. The main effect of group (PD vs. controls) was not significant in any of the repeated-measures ANOVAs (all $ps > 0.28$ and all $Fs < 1.21$), suggesting that there were not any significant between-groups differences in

Table 2
Schizotypy, Impulsivity, Divergent Thinking, and Verbal Fluency at Baseline and Follow-Up

	Baseline		Follow-up		Session × Group			
	PD	Controls	PD	Controls	$F(1, 35)$	p	η_p^2	Post hoc
Unusual Experiences	8.1 (4.4)	9.1 (4.7)	14.0 (6.4)	9.6 (4.7)	15.49	<.001	0.307	PD.1 < PD.2**
Introvertive Anhedonia	5.9 (3.1)	5.4 (2.8)	5.7 (2.6)	5.6 (2.9)	1.08	0.307	0.030	—
Cognitive Disorganization	8.4 (3.4)	8.2 (3.1)	9.1 (3.0)	8.4 (3.8)	0.41	0.840	0.001	—
Impulsive Nonconformity	7.6 (3.7)	8.2 (3.9)	8.5 (3.0)	8.1 (3.1)	3.98	0.054	0.102	—
Trait impulsivity	59.5 (14.0)	61.4 (12.1)	65.4 (12.0)	61.8 (10.5)	6.82	0.013	0.163	PD.1 < PD.2**
DT: Originality	4.9 (3.8)	5.2 (3.0)	5.7 (6.0)	5.5 (3.1)	0.27	0.608	0.008	—
DT: Fluency	6.4 (3.0)	7.1 (3.4)	9.6 (4.7)	7.6 (3.3)	3.84	0.058	0.099	—
DT: Flexibility	6.0 (3.9)	5.9 (3.3)	9.1 (5.1)	6.8 (3.4)	3.26	0.080	0.085	—
Letter fluency	42.2 (10.2)	44.4 (9.4)	41.1 (10.9)	44.6 (9.2)	0.44	0.509	0.013	—

Note. PD = Parkinson's disease; DT = divergent thinking, which was measured with the Just Suppose subtest of the Torrance Tests of Creative Thinking. Data indicate means, with standard deviations in parentheses. Dimensions of schizotypy, as reflected by the Oxford-Liverpool Inventory of Feelings and Experiences subscales, are shown in the first four rows. Trait impulsivity was measured with the Barratt Impulsiveness Scale. Letter fluency was measured with the F-A-S test. Repeated measures analyses of variance were performed to explore session and group effects (see Method for details). F and p values and effect sizes (η_p^2) are reported for Session × Group interactions. For significant interactions, the results of post hoc pairwise comparisons (with Bonferroni adjustment) are shown in the last column, with numbers referring to baseline (1) and follow-up (2).
** $p < .01$.

terms of schizotypy, trait impulsivity, divergent thinking, and letter fluency, when data were collapsed across sessions.

The statistics of the Session × Group interactions from the repeated-measures ANOVAs for each measurement are reported in Table 2. The interaction was significant for the Unusual Experiences score and for trait impulsivity (BIS-11 score). Post hoc tests revealed that, in each case, there was a significant increase from baseline to follow-up in the PD group, but not in the control group. The interactions were marginally significant ($0.05 < p < .1$) for the Impulsive Nonconformity score, and the fluency and the flexibility scores of the divergent thinking task. Laterality of symptom onset did not influence significantly between-session change in schizotypy, impulsivity, or divergent thinking (predicting follow-up scores from baseline in linear regressions, all ps > 0.11 for the interactions between PD and laterality).

Individual Differences in Between-Session Changes

Multiple linear regressions. The results of the regression analyses are summarized in Table 5, 6 and 7. All models were significant (all ps < 0.01). The total CAQ score was highly skewed; therefore, a log-transformed score was used in the regres-

Table 3
Spearman's Rho Rank Correlation Coefficients Between Pre and Post Measures Among Patients With Parkinson's Disease (N = 18)

	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. IQ	0.32	0.21	0.19	−0.21	−0.17	−0.08	0.01	**−0.65**	−0.30	**−0.66**	**−0.60**	0.02	0.15	−0.15	0.35	0.07	−0.06	**0.82**	0.45
2. CAQ		*0.54*	0.39	0.02	0.04	−0.26	−0.41	−0.16	*0.49*	−0.16	0.20	0.45	0.32	0.18	0.42	0.34	**0.66**	0.43	0.20
3. UnEx1			0.41	−0.29	−0.33	−0.39	*−0.59*	−0.39	0.21	−0.33	−0.02	*0.50*	*0.53*	0.11	0.29	*0.54*	0.23	0.41	0.28
4. UnEx2				−0.12	0.00	−0.30	−0.33	0.14	0.33	0.18	0.15	*0.57*	**0.60**	0.26	0.45	*0.53*	0.19	0.31	0.24
5. IntAnh1					**0.89**	0.24	0.12	0.23	−0.26	0.27	0.09	0.14	0.03	*−0.51*	−0.31	0.13	0.11	−0.28	*−0.50*
6. IntAnh2						0.34	0.21	0.30	−0.18	0.38	0.24	0.21	0.06	−0.27	−0.01	0.12	0.26	−0.28	−0.38
7. CogDis1							**0.82**	0.28	−0.09	0.30	0.12	−0.39	**−0.60**	−0.25	−0.01	**−0.61**	0.05	−0.15	0.12
8. CogDis2								0.18	−0.20	0.25	0.03	*−0.52*	**−0.69**	−0.35	−0.04	**−0.68**	−0.20	−0.24	−0.01
9. ImpNon1									*0.52*	**0.94**	**0.73**	−0.06	−0.19	0.29	0.00	−0.10	0.13	*−0.48*	−0.15
10. ImpNon2										0.41	**0.78**	0.15	0.07	*0.58*	0.33	0.09	0.36	−0.15	0.06
11. BIS1											**0.73**	0.03	−0.19	0.26	0.10	−0.06	0.14	*−0.46*	−0.13
12. BIS2												0.12	−0.05	*0.48*	0.25	0.09	0.32	*−0.51*	−0.17
13. Orig1													**0.80**	0.05	0.19	**0.66**	0.35	0.17	0.02
14. Orig2														0.16	0.21	**0.77**	0.14	0.15	−0.08
15. Flu1															*0.58*	0.20	0.24	−0.01	0.21
16. Flu2																0.09	0.15	0.24	0.14
17. Flex1																	0.31	0.20	0.04
18. Flex2																		0.14	0.29
19. LetterFlu1																			**0.76**
20. LetterFlu2																			

Note. IQ = intelligence measured with the Wechsler Adult Intelligence Scale; CAQ = Creative Achievement Questionnaire score; UnEx = Unusual Experiences; CogDis = Cognitive Disorganization; ImpNon = Impulsive Nonconformity; IntAnh = Introvertive Anhedonia; BIS = Barratt Impulsiveness Scale; Orig = originality of divergent thinking (DT); Flu = fluency of DT; Flex: flexibility of DT; LetterFlu = number of words generated in the F-A-S test. Numbers after variable names indicate baseline (1) and follow-up (2). $p < .05$ are highlighted in *italics*, and $p < .01$ are highlighted in **bold**.

Table 4
Spearman's Rho Rank Correlation Coefficients Between Pre and Post Measures Among Healthy Controls (N = 19)

	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. IQ	*0.47*	0.38	0.44	−0.04	−0.06	0.00	−0.23	0.26	0.10	0.09	0.12	0.29	0.30	0.30	−0.01	0.09	0.08	**0.66**	*0.55*
2. CAQ		−0.04	−0.08	−0.10	−0.12	0.32	0.17	−0.17	−0.18	−0.23	−0.20	**0.60**	**0.71**	0.03	−0.04	0.37	−0.24	0.28	0.36
3. UnEx1			**0.92**	0.04	0.19	−0.28	−0.31	−0.15	−0.20	−0.18	−0.16	−0.05	−0.13	0.23	0.29	−0.15	0.00	−0.03	0.11
4. UnEx2				0.12	0.29	−0.40	*−0.46*	−0.16	−0.22	−0.10	−0.09	−0.15	−0.24	0.28	0.21	−0.26	−0.03	0.06	0.17
5. IntAnh1					**0.82**	−0.12	−0.06	−0.38	−0.40	−0.44	−0.45	−0.27	−0.10	0.00	−0.24	−0.05	−0.03	0.16	0.42
6. IntAnh2						−0.38	−0.35	−0.38	−0.42	−0.27	−0.30	−0.27	−0.13	−0.07	−0.16	−0.1	0.09	0.09	0.33
7. CogDis1							**0.92**	−0.17	−0.12	−0.20	−0.11	0.04	−0.01	−0.18	−0.23	−0.3	*−0.56*	0.15	0.32
8. CogDis2								−0.20	−0.07	−0.29	−0.21	−0.04	−0.10	−0.09	−0.21	−0.21	*−0.49*	−0.11	0.09
9. ImpNon1									**0.95**	**0.66**	**0.62**	−0.01	0.05	0.09	0.10	0.23	0.44	0.11	−0.14
10. ImpNon2										*0.54*	*0.50*	−0.06	−0.02	0.11	0.12	0.26	0.40	−0.03	−0.26
11. BIS1											**0.97**	−0.04	−0.10	0.01	0.07	−0.06	0.33	−0.15	−0.36
12. BIS2												−0.11	−0.15	−0.04	0.07	−0.18	0.22	−0.16	−0.31
13. Orig1													**0.81**	0.32	0.11	**0.59**	0.17	0.06	−0.12
14. Orig2														0.19	0.24	**0.73**	0.25	0.14	0.06
15. Flu1															**0.58**	0.29	0.21	−0.09	−0.13
16. Flu2																0.28	0.36	−0.21	−0.21
17. Flex1																	**0.64**	−0.01	−0.21
18. Flex2																		0.07	−0.21
19. LetterFlu1																			**0.83**
20. LetterFlu2																			

Note. IQ = intelligence measured with the Wechsler Adult Intelligence Scale; CAQ = Creative Achievement Questionnaire score; UnEx = Unusual Experiences; CogDis = Cognitive Disorganization; ImpNon = Impulsive Nonconformity; IntAnh = Introvertive Anhedonia; BIS = Barratt Impulsiveness Scale; Orig = originality of divergent thinking (DT); Flu = fluency of DT; Flex: flexibility of DT; LetterFlu = number of words generated in the F-A-S test. Numbers after variable names indicate baseline (1) and follow-up (2). $p < .05$ are highlighted in *italics*, and $p < .01$ are highlighted in **bold**.

sions (following Silvia, Nusbaum, Berg, Martin, & O'Connor, 2009).

Follow-up originality scores were significantly and positively predicted by baseline originality scores, PD and the interaction between Unusual Experiences and PD in the third step ($\Delta R^2 = 0.05$), $F(1, 32) = 5.62$, $p = .024$, reflecting that patients with higher levels of positive schizotypy at pretreatment are more likely to show improvement of originality at posttreatment. Moreover, baseline originality and Cognitive Disorganization scores significantly and negatively predicted follow-up originality scores in the second step ($\Delta R^2 = 0.08$), $F(2, 33) = 4.69$, $p = .016$. This suggests that disorganized schizotypy at baseline was related to a decrease in originality scores in the whole sample. In the third step, however, both Cognitive Disorganization and the interaction term between Cognitive Disorganization and PD were not significant ($\Delta R^2 = 0.02$), $F(1, 32) = 2.58$, $p = .118$. This pattern could implicate a general negative effect of disorganized schizotypy on change in originality, although the lack of a significant effect with regard PD might be due to power problems. No other models predicting follow-up originality scores improved significantly neither in the second nor the third step (all $ps > 0.1$, Table 5).

Follow-up fluency scores were significantly and positively predicted by baseline fluency scores, intelligence and PD in the second step ($\Delta R^2 = 0.14$), $F(2, 33) = 4.25$, $p = .023$. The model marginally improved when extended with the interaction between intelligence and PD ($\Delta R^2 = 0.05$), $F(1, 32) = 3.04$, $p = .091$. Although this interaction failed to reach statistical significance, it is noteworthy that the single intelligence term turned highly nonsignificant ($p > .8$) and negative in the third step, tempting one to speculate that patients drove the significant effect observed in the second step. This would imply that patients with higher baseline intelligence could be more likely to demonstrate increased fluency at follow-up. The (borderline) significant effects of PD tended to improve four other models in the second steps, while failing to do so in one case. No other models predicting follow-up fluency scores improved significantly in the third steps (all $ps > 0.1$, Table 6).

Follow-up flexibility scores were significantly and positively predicted by baseline flexibility scores and the interaction between lifetime creative achievement and PD in the third step ($\Delta R^2 = 0.10$, $F(2, 33) = 6.75$, $p = .014$), implying that patients with greater lifetime creative achievement could be expected to show elevated flexibility after treatment. What is more, follow-up flexibility scores were significantly and positively predicted by baseline flexibility scores and the interaction between Cognitive Disorganization and PD in the third step ($\Delta R^2 = 0.08$), $F(1, 32) = 5.02$, $p = .032$, suggesting that patients who were more disorganized before the beginning of the pharmacotherapy demonstrated a larger increase in flexibility. Finally, follow-up flexibility scores were significantly and positively predicted by baseline flexibility scores, Impulsive Nonconformity and PD in the second step ($\Delta R^2 = 0.17$), $F(2, 33) = 5.93$, $p = .006$. Extending this model with the interaction term did not lead to any improvement ($\Delta R^2 < 0.01$), $F(1, 32) = 0.27$, $p = .609$. The nonsignificant interaction and the significant positive effect of baseline flexibility and Impulsive Nonconformity together suggested that impulsive schizotypy was related to the change of flexibility scores exclusively in the control group. None of the other models predicting follow-up flexibility scores improved significantly in the third steps (all $ps > 0.1$, Table 7).

Discussion

In this study, we longitudinally examined some potential factors behind emerging creativity in PD. We focused on divergent thinking ability, an indicator of creative potential (Amabile, 1983;

Table 5
Individual Differences in Between-Session Change: Predictors of the Follow-Up Originality Score

Step 2	β	*t*	*p*	Model summary	Step 3	β	*t*	*p*	Model summary
Orig	0.77	7.65	<.001	$F(3, 33) = 22.35^{**}$, $R^2_{adj} = .64$,	Orig	0.78	7.65	<.001	$F(4, 32) = 16.33^{**}$, $R^2_{adj} = .64$,
PD	−0.04	−0.44	.661	$\Delta R^2 = .03$	PD	−0.82	−0.84	.410	$\Delta R^2 = .01$
IQ	0.17	1.69	.101		IQ	0.06	0.34	.739	
					PD × IQ	0.78	0.79	.433	
Orig	0.71	6.00	<.001	$F(3, 33) = 21.40^{**}$, $R^2_{adj} = .63$,	Orig	0.71	6.04	<.001	$F(4, 32) = 16.42^{**}$, $R^2_{adj} = .63$,
PD	−0.05	−0.47	.638	$\Delta R^2 = .02$	PD	−0.22	−1.16	.253	$\Delta R^2 = .01$
CAQ	0.16	1.35	.188		CAQ	0.05	0.35	.728	
					PD × CAQ	0.22	1.08	.288	
Orig	0.76	7.37	<.001	$F(3, 33) = 22.27^{**}$, $R^2_{adj} = .64$,	Orig	0.69	6.93	<.001	$F(4, 32) = 20.45^{**}$, $R^2_{adj} = .68$,
PD	−0.04	−0.39	.698	$\Delta R^2 = .03$	PD	−0.49	−2.31	.027	$\Delta R^2 = .05^{*}$
UnEx	0.17	1.66	.107		UnEx	−0.02	−0.19	.847	
					PD × UnEx	0.53	2.37	.024	
Orig	0.79	7.56	<.001	$F(3, 33) = 19.71^{**}$, $R^2_{adj} = .61$,	Orig	0.81	7.38	<.001	$F(4, 32) = 14.51^{**}$, $R^2_{adj} = .60$,
PD	−0.05	−0.52	.606	$\Delta R^2 = .00$	PD	0.17	0.37	.716	$\Delta R^2 = .00$
IntAnh	0.00	0.03	.977		IntAnh	0.06	0.40	.693	
					PD × IntAnh	−0.24	−0.50	.620	
Orig	0.74	7.75	<.001	$F(3, 33) = 28.12^{**}$, $R^2_{adj} = .69$,	Orig	0.70	7.33	<.001	$F(4, 32) = 22.74^{**}$, $R^2_{adj} = .71$,
PD	−0.05	−0.52	.606	$\Delta R^2 = .08^{*}$	PD	0.34	1.32	.197	$\Delta R^2 = .02$
CogDis	−0.28	−3.01	.005		CogDis	−0.13	−0.96	.345	
					PD × CogDis	−0.46	−1.61	.118	
Orig	0.79	7.53	<.001	$F(3, 33) = 19.72^{**}$, $R^2_{adj} = .61$,	Orig	0.81	7.66	<.001	$F(4, 32) = 15.36^{**}$, $R^2_{adj} = .61$,
PD	−0.06	−0.53	.601	$\Delta R^2 = .00$	PD	0.21	0.86	.395	$\Delta R^2 = .02$
ImpNon	−0.01	−0.12	.904		ImpNon	0.10	0.73	.472	
					PD × ImpNon	−0.31	−1.20	.238	

Note. Orig = originality of divergent thinking; PD = Parkinson's disease (dummy variable coding group membership, PD = 1); IQ = intelligence measured with the Wechsler Adult Intelligence Scale; CAQ = log-transformed Creative Achievement Questionnaire score; UnEx = Unusual Experiences; IntAnh = Introvertive Anhedonia; CogDis = Cognitive Disorganization; ImpNon = Impulsive Nonconformity. The model where the baseline originality score was the only independent variable (Step 1) was significant: $F(1, 35) = 61.92^{**}$, $R^2_{adj} = .63$, β = .80, $t = 7.87$, $p < .001$. All predictors were measured at baseline.
* $p < .05$. ** $p < .01$.

Batey & Furnham, 2006; Plucker & Makel, 2010; Runco & Acar, 2012). We found trends suggesting that dopamine agonists might have boosted the fluency and the flexibility of verbally assessed divergent thinking in PD. Convergent thinking and verbal fluency were spared in the PD group, suggesting intact executive functions. What is more, we found no evidence indicative of dopaminergic therapy affecting verbal fluency, suggesting that enhanced divergent thinking observed in PD is not strongly tied to increased broad retrieval ability (Silvia et al., 2013). Positive schizotypal traits (i.e., the tendency for unusual experiences) and impulsivity also increased in the PD group after dopaminergic medications, which is consistent with previous results (Cools, Barker, Sahakian, & Robbins, 2003; Nagy et al., 2012; Ondo & Lai, 2008).

Our study casts light on which factors could modulate dopaminergic drugs' effect on creativity: In the PD group, change in originality of verbal divergent thinking was positively associated with positive schizotypy. This relationship harmonizes with studies of nonclinical populations, which connected divergent thinking and creativity with schizotypal traits in the same pattern (Acar & Sen, 2013; Batey & Furnham, 2008; Claridge & Blakey, 2009; Nelson & Rawlings, 2010; Nettle & Clegg, 2006). Interestingly, disorganized schizotypy was positively linked to change in flexibility in the PD group: Patients who were more cognitively disorganized at baseline were more likely to show increased flexibility of divergent thinking after dopaminergic therapy.

Furthermore, we could positively relate change in flexibility of verbal divergent thinking to lifetime creative achievements. Interestingly, those with higher lifetime creativity were more susceptible to the divergent thinking booster effect of dopaminergic drug. Eminently creative patients were more likely to demonstrate increased flexibility of verbal divergent thinking after treatment (while general verbal fluency did not change significantly). Lifetime creative achievement previously has been related to excellent intellectual abilities (Carson et al., 2003; Jauk et al., 2013; Kell et al., 2013; Kéri, 2011), decreased latent inhibition (Carson et al., 2003; Kéri, 2011), high openness (Carson et al., 2005; Silvia et al., 2009), and rich proximal social network (Kéri, 2011). Therefore, we suggest that a high score on the CAQ might reflect an optimal blend of low latent inhibition, high intelligence and openness, and strong social support, which seem to provide ideal circumstances for dopaminergic stimulation to turn into increased divergent thinking. This conjecture is in line with the hypothesis that reduced latent inhibition—potentially induced by dopamine agonists (Swerdlow et al., 2003)—is more likely to translate into creativity in the presence of excellent intellectual abilities (Carson et al., 2003; Kéri, 2011). Although the trend suggesting a correlation between intelligence and improvement of fluency of divergent thinking in PD could be seen to parallel this rationale, this marginally significant result should be cautiously interpreted. Attention has previously been drawn to lifetime creativity in the PD literature, as some cases suggested that a creative profession might be a risk factor for dopamine dysregulation syndrome (Schwingenschuh et al., 2010). The precise relevance of correlates of cre-

Table 6
Individual Differences in Between-Session Change: Predictors of the Follow-Up Fluency Score

Step 2	β	*t*	*p*	Model summary	Step 3	β	*t*	*p*	Model summary
Flu	0.58	4.50	<.001	$F(3, 33) = 9.61^{**}$, $R^2_{adj} = .42$,	Flu	0.62	4.90	<.001	$F(4, 32) = 8.40^{**}$, $R^2_{adj} = .45$,
PD	0.28	2.20	.035	$\Delta R^2 = .14^{*}$	PD	−1.84	−1.50	.143	$\Delta R^2 = .05^{+}$
IQ	0.26	2.05	.049		IQ	−0.05	−0.22	.830	
					PD × IQ	2.14	1.74	.091	
Flu	0.58	4.43	<.001	$F(3, 33) = 8.42^{**}$, $R^2_{adj} = .38$,	Flu	0.57	4.41	<.001	$F(4, 32) = 6.99^{**}$, $R^2_{adj} = .40$,
PD	0.28	2.14	.040	$\Delta R^2 = .10^{+}$	PD	0.00	0.01	.995	$\Delta R^2 = .03$
CAQ	0.19	1.43	.162		CAQ	0.02	0.09	.929	
					PD × CAQ	0.36	1.41	.170	
Flu	0.55	4.11	<.001	$F(3, 33) = 8.53^{**}$, $R^2_{adj} = .39$,	Flu	0.56	4.10	<.001	$F(4, 32) = 6.33^{**}$, $R^2_{adj} = .37$,
PD	0.28	2.15	.039	$\Delta R^2 = .11^{+}$	PD	0.15	0.51	.614	$\Delta R^2 = .00$
UnEx	0.20	1.50	.142		UnEx	0.14	0.76	.455	
					PD × UnEx	0.16	0.53	.599	
Flu	0.57	4.22	<.001	$F(3, 33) = 7.99^{**}$, $R^2_{adj} = .37$,	Flu	0.60	4.23	<.001	$F(4, 32) = 6.03^{**}$, $R^2_{adj} = .36$,
PD	0.27	2.04	.050	$\Delta R^2 = .09^{+}$	PD	−0.13	−0.22	.824	$\Delta R^2 = .01$
IntAnh	−0.15	−1.14	.265		IntAnh	−0.26	−1.28	.209	
					PD × IntAnh	0.44	0.71	.482	
Flu	0.60	4.28	<.001	$F(3, 33) = 7.28^{**}$, $R^2_{adj} = .34$,	Flu	0.60	4.34	<.001	$F(4, 32) = 5.94^{**}$, $R^2_{adj} = .35$,
PD	0.26	1.95	.059	$\Delta R^2 = .07^{+}$	PD	−0.18	−0.47	.645	$\Delta R^2 = .03$
CogDis	0.00	0.02	.987		CogDis	−0.18	−0.90	.377	
					PD × CogDis	0.51	1.25	.221	
Flu	0.59	4.27	<.001	$F(3, 33) = 7.29^{**}$, $R^2_{adj} = .34$,	Flu	0.62	4.46	<.001	$F(4, 32) = 6.02^{**}$, $R^2_{adj} = .36$,
PD	0.27	1.96	.059	$\Delta R^2 = .07$	PD	0.65	2.03	.051	$\Delta R^2 = .03$
ImpNon	0.02	0.13	.895		ImpNon	0.18	0.98	.336	
					PD × ImpNon	−0.44	−1.32	.198	

Note. Flu = fluency of divergent thinking; PD = Parkinson's disease (dummy variable coding group membership, PD = 1); IQ = intelligence measured with the Wechsler Adult Intelligence Scale; CAQ = log-transformed Creative Achievement Questionnaire score; UnEx = Unusual Experiences; IntAnh = Introvertive Anhedonia; CogDis = Cognitive Disorganization; ImpNon = Impulsive Nonconformity. The model where the baseline fluency score was the only independent variable (Step 1) was significant: $F(1, 35) = 17.14^{**}$, $R^2_{adj} = .31$, β = .57, $t = 4.14$, $p < .001$. All predictors were measured at baseline.
$^{+}$ $p < .1$. * $p < .05$. ** $p < .01$.

ative achievement to drug side effects in PD should be clarified in future research.

To date, several case studies have reported the unfolding of real-life creativity related to dopaminergic therapy in PD (Canesi et al., 2012; Chatterjee et al., 2006; Joutsa et al., 2012; Kulisevsky et al., 2009; López-Pousa et al., 2012; Schrag & Trimble, 2001; Walker et al., 2006). A linkage between improved creativity and impulse control problems has been implied (Joutsa et al., 2012; Kulisevsky et al., 2009; Schrag & Trimble, 2001; Walker et al., 2006), and engaging in creative activities could also serve as a psychological coping mechanism (Chatterjee et al., 2006; Kulisevsky et al., 2009; López-Pousa et al., 2012). So far, two systematic studies have addressed the creativity side effect of dopaminergic therapy in PD. Drago et al. (2009) reported decreased fluency in a verbal divergent thinking task only in patients with right hemibody onset, relative to the controls. Patients with left hemibody onset were comparable to the controls on all aspects of divergent thinking. Data indicated that the results were not due to a general deficit of verbal fluency. However, the left hemibody onset group had more severe motor symptoms. We found no differences in terms of between-session changes between patients with left and right hemibody onset, although the sample size was small to obtain sound conclusions regarding laterality.

Canesi et al. (2012) found that patients who became creative after treatment performed similarly to control subjects on a divergent thinking task, while PD patients not developing new creative potentials had reduced performance. Canesi et al. (2012) had not examined patients who were professional or hobby artists, while our sample was heterogeneous with respect to real-life creative achievement.

To the best of our knowledge, this is the first attempt to longitudinally study changes in divergent thinking in relation to schizotypy and impulsivity during dopaminergic therapy in PD. Similarly to two systematic studies conducted before, we examined cognitively preserved patients, although our sample was younger (mean age: 47.6 vs. 61.0, Canesi et al., 2012, and 70.8, Drago et al., 2009) consisting of new-onset patients receiving their first lifetime dopaminergic medication. Pharmacotherapy was confined to dopamine agonists. These differences between the studies may explain the heterogeneity of findings.

The most important limitation of the study is the small sample size, which did not allow more sophisticated statistics with more predictors in the multiple regression analyses. Additionally, as application of the Torrance Test of Creative Thinking in research has recently been strongly debated (Baer, 2011a, 2011b; but also see Kim, 2011a, 2011b) it should be noted that our findings are restricted to particular aspects of divergent thinking in the verbal domain. A traditional method was used to evaluate divergent thinking (Torrance, 1974), which received criticisms for confounding originality with fluency and a subjective scoring technique has been proposed (Silvia et al., 2008). Nevertheless, the weak and nonsignificant correlations between originality and fluency scores in this study seem to relax this concern, together with empirical arguments in defense of the traditional scoring approach (see Runco, 2008). Finally, future studies should explore if the yet obtained results generalize to divergent thinking in the figural

Table 7
Individual Differences in Between-Session Change: Predictors of the Follow-Up Flexibility Score

Step 2	β	*t*	*p*	Model summary	Step 3	β	*t*	*p*	Model summary
Flex	0.61	4.67	<.001	$F(3, 33) = 8.74^{**}$, $R^2_{adj} = .39$,	Flex	0.61	4.65	<.001	$F(4, 32) = 6.51^{**}$, $R^2_{adj} = .38$,
PD	0.27	2.09	.045	$\Delta R^2 = .07$	PD	1.02	0.80	.429	$\Delta R^2 = .01$
IQ	0.00	0.04	.972		IQ	0.11	0.50	.621	
					PD × IQ	−0.75	−0.59	.559	
Flex	0.62	4.45	<.001	$F(3, 33) = 8.76^{**}$, $R^2_{adj} = .39$,	Flex	0.58	4.47	<.001	$F(4, 32) = 9.40^{**}$, $R^2_{adj} = .48$,
PD	0.27	2.06	.047	$\Delta R^2 = .07$	PD	−0.21	−0.96	.345	$\Delta R^2 = .10^{*}$
CAQ	−0.03	−0.19	.853		CAQ	−0.31	−1.84	.075	
					PD × CAQ	0.63	2.60	.014	
Flex	0.61	4.66	<.001	$F(3, 33) = 8.77^{**}$, $R^2_{adj} = .39$,	Flex	0.63	4.46	<.001	$F(4, 32) = 6.43^{**}$, $R^2_{adj} = .38$,
PD	0.27	2.06	.048	$\Delta R^2 = .07$	PD	0.36	1.20	.241	$\Delta R^2 = .00$
UnEx	−0.03	−0.22	.825		UnEx	0.01	0.06	.956	
					PD × UnEx	−0.11	−0.34	.739	
Flex	0.61	4.66	<.001	$F(3, 33) = 8.75^{**}$, $R^2_{adj} = .39$,	Flex	0.60	4.53	<.001	$F(4, 32) = 6.40^{**}$, $R^2_{adj} = .37$,
PD	0.27	2.08	.045	$\Delta R^2 = .07$	PD	0.12	0.22	.830	$\Delta R^2 = .00$
IntAnh	0.02	0.12	.903		IntAnh	−0.02	−0.13	.901	
					PD × IntAnh	0.16	0.28	.785	
Flex	0.62	4.18	<.001	$F(3, 33) = 8.74^{**}$, $R^2_{adj} = .39$,	Flex	0.65	4.66	<.001	$F(4, 32) = 8.61^{**}$, $R^2_{adj} = .46$,
PD	0.27	2.09	.045	$\Delta R^2 = .07$	PD	−0.46	−1.32	.197	$\Delta R^2 = .08^{*}$
CogDis	0.01	0.06	.951		CogDis	−0.28	−1.46	.153	
					PD × CogDis	0.85	2.24	.032	
Flex	0.55	4.56	<.001	$F(3, 33) = 12.70^{**}$, $R^2_{adj} =$	Flex	0.55	4.50	<.001	$F(4, 32) = 9.38^{**}$, $R^2_{adj} = .48$,
PD	0.30	2.51	.017	$.49$, $\Delta R^2 = .17^{**}$	PD	0.43	1.53	.137	$\Delta R^2 = .00$
ImpNon	0.31	2.57	.015		ImpNon	0.37	2.22	.034	
					PD × ImpNon	−0.15	−0.52	.609	

Note. Flex = flexibility of divergent thinking; PD = Parkinson's disease (dummy variable coding group membership, PD = 1); IQ = intelligence measured with the Wechsler Adult Intelligence Scale; CAQ = log-transformed Creative Achievement Questionnaire score; UnEx = Unusual Experiences; IntAnh = Introvertive Anhedonia; CogDis = Cognitive Disorganization; ImpNon = Impulsive Nonconformity. The model where the baseline flexibility score was the only independent variable (Step 1) was significant: $F(1, 35) = 20.46^{**}$, $R^2_{adj} = .35$, β = .61, $t = 4.52$, $p < .001$. All predictors were measured at baseline.
* $p < .05$. ** $p < .01$.

domain and to engagement in real life creative activities as well (e.g., Batey & Furnham, 2008).

Conclusions

We found individual differences relevant to increasing verbal divergent thinking in a group of cognitively preserved PD patients after 12 weeks of dopamine agonist therapy. Enhancement of divergent thinking might be one of the factors underlying the emergence of creative potentials in PD. The results suggested that positive and disorganized schizotypy, and lifetime creative achievements can be de novo predictors of change in divergent thinking in PD. Furthermore, our study replicated previous findings by documenting elevated impulsivity and positive schizotypy in PD at follow-up. The results offer an explanation for individual differences in drug-induced creativity, a fascinating side effect of dopaminergic therapy in PD, and also shed light on the biological aspects of divergent thinking.

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