Tonic Noradrenergic Activity Modulates Explorative Behavior and Attentional Set Shifting: Evidence from Pupillometry and Gaze Pattern Analysis

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Abstract

A constant task for every living organism is to decide whether to exploit rewards associated with current behavior or to explore the environment for more rewarding options. Current empirical evidence indicates that exploitation is related to phasic whereas exploration to tonic firing mode of noradrenergic neurons in the locus coeruleus. In humans, this exploration-exploitation trade-off is subserved by the ability to flexibly switch attention between task-related and task-irrelevant information. Here, we investigated whether this function, called attentional set-shifting, is related to exploration and tonic noradrenergic discharge. We measured pretrial, baseline pupil dilation, proved to be strongly correlated with the activity of the locus coeruleus, while human participants took part in well-known tasks of attentional set shifting. In Experiment 1, the Wisconsin Card Sorting Task, whereas in Experiment 2, the Intra/Extradimensional Set Shifting Task was used. Both tasks require participants to choose between different compound stimuli based on feedback provided for their previous decisions. During the task, stimulus-reward contingencies change periodically, thus participants are repeatedly required to reassess which stimulus-features are relevant (i.e. they shift their attentional set). Our results showed that baseline pupil diameter steadily decreased when the stimulus-reward contingencies were stable, whereas they suddenly increased, when these contingencies changed. Analysis of looking patterns also confirmed the presence of exploratory behavior during attentional set shifting. Thus, our results suggest that tonic firing mode of noradrenergic neurons in the locus coeruleus is implicated in attentional set shifting, as it regulates the amount of exploration.

Keywords: LC/NA system, exploration/exploitation trade-off, Intra/Extradimensional Set Shifting Task, Wisconsin Card Sorting Task, pupillometry

Tonic Noradrenergic Activity Modulates Explorative Behavior and Attentional Set Shifting: Evidence from Pupillometry and Gaze Pattern Analysis

One of the fundamental tasks during the selection of appropriate behavior is a decision between two strategies: to exploit current rewards or to explore the environment for other sources of reward. This decision represents a trade-off between exploiting known rewards versus leaving those rewards for potentially better outcomes (Cohen, McLure, & Yu, 2007; Hills et al., 2015). One factor driving this trade-off is the temporal change of reward values associated with different stimuli and behavioral options.

In an ever changing environment with complex stimuli, this updating of stimulus-reward contingencies requires the ability to flexibly switch the focus of attention between different aspects of these stimuli. This ability is termed attentional set shifting, and is a key aspect of higher order cognition and cognitive flexibility. It is frequently assessed by the Wisconsin Card Sorting Task (henceforth WCST; Berg, 1948; Heaton, Curtiss, & Tuttle, 1993), a well-known diagnostic tool of frontal dysfunctions (Milner, 1963). An alternative task for assessing attentional set shifting is the Intra/Extradimensional Set Shifting Task (henceforth IEDT), which permits to disentangle different aspects of attentional set shifting (Downes, Roberts, Sahakian, Evenden, Morris, & Robbins, 1989; Owen et al., 1992). This task is part of the Cambridge Automated Test Battery (henceforth CANTAB), a frequently used neuropsychological diagnostic tool (Fray, Robbins, & Sahakian, 1996)

Despite differences in task design, the crucial features of the WCST and the IEDT are similar: participants have to choose between compound stimuli (i.e. complex stimuli characterized by distinct stimulus-dimensions). Their decisions are rewarded according to a hidden rule, and based on feedback received for their choices, they have to figure out which feature of the compound stimuli is rewarded. After participants acquired the rule, as indicated

by consecutive correct choices, the rule changes, and participants are required to reassess which stimulus-features are relevant (i.e. they have to shift their attentional set).

Studies using both the WCST and the IEDT generated comprehensive evidence suggesting that attentional set shifting is impaired in several psychiatric and neurological conditions, including schizophrenia (Heinricks & Zakzanis, 1998; Jazbec, Pantelis, Robbins, Weickert, Weinberger, & Goldberg, 2007; Pantelis et al., 2009; Reichenberg & Harvey, 2007), obsessive–compulsive disorder (Chamberlain, Fineberg, Blackwell, Robbins, & Sahakian, 2006; Demeter, Racsmány, Csigó, Harsányi, Döme, & Németh, 2013; Roh et al., 2005), Parkinson's Disease (Kudlicka, Claire, & Hindle, 2011, Owen et al., 1992), and Attention Deficit Hyperactivity Disorder (Gau & Shang, 2010; Sergeant, Geurts, & Oosterlan, 2002). Neuronal underpinnings of attentional set shifting have also been examined. The WSCT is a sensitive measure of prefrontal cortex dysfunctions, with reliable deficits related to prefrontal lesions (see. e.g. Grafman, Jonas, & Salazar, 1990; Janowsky, Shimamura, Kritchevsky, & Squire, 1989; Milner, 1963). Functional neuroimaging studies implicated most notably dorsolateral prefrontal cortex activation during the WCST, but posterior association areas and subcortical structures are also involved (for review sees Nyhus & Barceló, 2009). Prefrontal involvement has also been shown for the IEDT (Dias, Robbins, & Roberts, 1996; Hampshire & Owen, 2006).

Rodent studies indicated that noradrenergic (henceforth NA) transmission in the prefrontal cortex is crucial for attentional set shifting (Lapiz & Morilak, 2006; McGaughy, Ross, & Eichenbaum, 2008; Tait, Brown, Farovik, Theobald, Dalley, & Robbins, 2007). Because both the WCST and the IEDT are important neuropsychological diagnostic tools, used in several psychiatric and neurological patient groups, the specific mechanisms between NA and attentional set shifting are important for translational research. Recent theories on

behavior control suggest that the link between NA transmission and attentional set shifting might be explained by the role of NA in regulating the amount of explorative behavior.

Noradrenergic Transmission and the Regulation of Exploration

The main source of NA transmission originates from the brain stem nucleus locus coeruleus (LC), and it innervates large parts of the neocortex. This network is often called the LC/NA system. Single-cell registration studies involving rodents and primates showed that phasic, burst-like activity of LC neurons accompanied presentation of task-relevant stimuli and responses. Furthermore, high tonic activity of LC neurons was related to erroneous performance suggesting that animals explored other environmental features instead of focusing on the current task (Aston-Jones, Rajkowski, Kubiak, & Alexinsky, 1994; Aston-Jones, Rajkowski, Kubiak, Valentino, & Shipley, 1996; Bouret & Sara, 2004; Usher, Cohen, Servan-Schreiber, Rajkowski, & Aston-Jones, 1999; for a review, see e.g. Ashton-Jones & Cohen, 2005).

Based on such results, partly similar theories emerged to explain the role of NA in the control of behavior. The adaptive gain theory (Ashton-Jones & Cohen, 2005) suggests that the burst-like activity of the LC/NA system is responsible for coordinating cortical networks which are necessary for the execution of a given response. This theory makes a distinction between the phasic and the tonic mode, the former being responsible for task exploitation and engagement with a current task, and the latter for exploration and task disengagement. The network reset hypothesis (Bouret & Sara, 2005), partly similarly to the adaptive gain theory, suggests that phasic NA is associated with resetting functional networks in the brain, which facilitates the formation of task-related networks. Finally, Yu and Dayan (2005), also in line with the adaptive gain theory, suggested that tonic, between-trial increases in NA transmission represent the level of unexpected uncertainty, signaling sudden, unexpected changes in the environment and triggering explorative behavior.

Although these theories are based on animal data, they can also be tested in humans with noninvasive methods. One candidate is pupillometry, as the size of the pupil is an indirect measure of LC activity (Ashton-Jones & Cohen, 2005; Joshi, Li, Kalwani, & Gold, 2016; Murphy, O'Connell, O'Sullivan, Robertson, & Balsters, 2014), most likely due to a common excitatory input source of both the LC and the Edinger-Westphal nucleus, which controls pupil size (Gilzenrat, Niewenhuis, Jepma, & Cohen, 2010; Joshi et al., 2015). The task-related phasic bursts of the LC correspond to task-evoked increases in pupil size which have long been considered as a correlate of cognitive processing and mental effort (Beatty, 1982; Kahneman & Beatty, 1966). Similarly to the phasic bursts of the LC, these task-evoked pupillary responses accompany task-related processing and are predictors of successful performance (Beatty, 1982). In contrast, pretrial pupil size, which reflects the tonic activity of the LC, has been shown to predict erroneous performance on the subsequent trial (Kristjansson, Stern, Brown, & Rohrbaugh, 2010; Unsworth & Robison, 2015; Smallwood et al., 2011).

Several studies have investigated the role of the LC/NA system in attentional and cognitive processing using pupillometry, and have found an association between task disengagement, erroneous performance, and off-task thought (e.g. Gilzenrat et al., 2010; Mittner, Boekel, Tucker, Turner, Heathcote, & Forstmann, 2013; Unsworth & Robinson, 2015). Less data is available on the adaptive aspects of exploration, when explorative tendencies are integral parts of behavior and contribute to successful task performance. For instance, Jepma and Nieuwenhuis (2011) found that high pretrial pupil size predicted explorative choices in a multiple-armed bandit task, where participants have to choose repeatedly from slot machines with changing reward values. Using a different task to assess analogical reasoning, Hayes and Petrov (2015) found that slow, tonic increase in pupil size was related to “mental foraging” and to transitions from exploitative to explorative problem

solving periods. Following this research line, in the present study, we made an attempt to contribute to the investigation of how tonic NA activity is related to successful performance in situations requiring exploration.

Attentional Set Shifting, Tonic NA and Exploration: The Current Study

Crucial requirement in both the WCST and the IEDT is to assess which stimulus-features are rewarded after a rule shift (i.e. when the stimulus-reward contingencies change). In these situations, participants have to explore the environment after sudden, unexpected changes to find a new way of behavior which leads to reinforcement. This explorative behavior is remarkably similar to the process described by the adaptive gain theory and by the proposal of Yu and Dayan (2005) as related to tonic, between-trial changes of NA transmission. This link between NA transmission and attentional set shifting has already been shown for rodents (Lapiz & Morilak, 2006; McGaughy et al., 2008; Tait et al., 2007), however, to the best of our knowledge, there are no human data focusing on this relationship.

To investigate this issue, we conducted two studies: we used the WCST in Study 1 and the IEDT in Study 2. We assessed the tonic activity of the LC/NA system, suggested to be related to exploration, by measuring pretrial pupil size (similarly to previous studies, see e.g. Jepma & Nieuwenhuis, 2011).

Our predictions were derived from theories of the LC/NA system and analysis of task demands before and after rule shifts. Since rule changes are triggered by a specific number of correct choices, indicating the knowledge of the correct stimulus-feature, the trials before a rule change constitute an exploitative phase. Here the stimulus-reward contingencies are identified and no exploration is required. In contrast, after rule changes, exploration and trial-error learning are required to identify the new rewarded stimulus feature.

Furthermore, the first correct choice in the sequence leading to a rule change should be accompanied by uncertainty, because it constitutes the end of the explorative phase. At this

point, the participant has just identified a to-be-chosen stimulus feature, and seeks reinforcement whether it is rewarded or not. With repeated positive feedback after choosing this feature, the responses will be accompanied by an increasing level of confidence. Thus, we predict that during the sequence of correct choices the LC/NA system will gradually shift from exploration to exploitation, and this should be reflected in a gradual decrease of pretrial pupil size. After the consecutive rule shift, the LC/NA system is expected to switch to a more explorative mode, to find the new rewarded stimulus features, and this will be reflected in a sudden increase of pretrial pupil size.

In order to gain converging evidence, the level of exploration was also assessed by monitoring the gaze pattern of participants. We aimed to observe whether explorative attentional patterns also accompany attentional set shifting. We assessed the relative amount of time participants looked at different stimulus-features (dwell time). We predicted that changes in these dwell times would mirror the pattern of pupil size changes: a gradual decrease before rule shift and a sudden increase after stimulus-reward contingencies change.

Finally, we also investigated changes in reaction time (RT) during the exploitative and the explorative phase. We predicted that the accumulation of learning during the exploitative phase will be associated with a decrease in RTs, whereas a sharp increase of RT will indicate explorative behavior after the change of stimulus-reward associations.

Method

Participants

Sixty-six participants took part in Study 1 (WCST). Four participants were excluded due to low data quality, and one participant due to data loss, resulting in a final sample size of 61 participants (30 female; age range: 18-29 years, M_{age} = 21.9, SD = 2.0). Participants were undergraduate students of different Hungarian universities, and were paid for participation.

In Study 2 (IEDT), 82 participants took part. Seven participants were excluded due to low eye-tracking data quality. Thus, the final sample size consisted of 75 participants (41 female; age range: 18-30 years, M_{age} = 23.0, *SD* = 2.8). Participants were undergraduate students of the Budapest University of Technology and Economics and participated for partial credit. All participants in both studies provided informed consent.

Study 1 - Wisconsin Card Sorting Test

We developed a computerized version of the task following the stimuli, standard administration procedure, and instruction of the test, described by Heaton et al. (1993). In each trial, the same four target cards appeared on the top of the screen. These cards depicted different symbols, differing in color, shape, and number. On the bottom middle part of the screen, a 5th card was shown, which was different in each trial of the task (see Figure 1A). For each trial, this 5th card could be matched to different target cards, based on similarity in different stimulus dimensions (e.g. in Figure 1A, participant could match the bottom card to the upper leftmost card based on number, and to the upper rightmost card based on color). However, only one sorting principle was correct at a time. The task of the participants was to figure out the correct sorting principle based on feedback received on previous trials. After 10 consecutive correct matches, the sorting principle changed. The sequence of the sorting principles was constant: at first color, then form and then number. This sequence was repeated twice, thus participants had to find the correct sorting principle six times. The test ended either after this or after matching 128 cards.

Before each trial, there was a pretrial period of 2.5 seconds, during which all symbols disappeared from the screen and participants were requested to fixate to the area of the 5th, to-be-matched card. This was followed by the presentation phase, where the four target cards and the to-be-matched 5th card were presented to the participants. We instructed participants to press the left button of the mouse if they made a decision on which card they would match

to the current to-be-matched card. Then, in the response phase, a cursor appeared and subjects had to move this cursor to the chosen target card and to press the left mouse button again. For this, they had one second. Using this procedure, we aimed to segregate fixation patterns and pupil size changes which are related to stimulus selection and response execution processes, respectively. Finally, there was a feedback phase of one second: either the text 'correct' with green ink or the text 'incorrect' with red ink appeared on the screen, indicating whether the participant matched the card according to the currently correct sorting principle.

<insert Figure 1 about here>

Study 2 - The Intra/Extradimensional Set Shifting Task

The stimulus dimensions of the IEDT used in the CANTAB are spatially overlapping (lines on a shape). These stimuli are not optimal for online tracking of attentional processes with an eye-tracker, because it is difficult to determine from the fixation pattern, which of the two stimulus-dimensions the subject is attending to. Thus, we developed a new version of the CANTAB task, which enabled us to track attention processes separately for the two stimulus dimensions. We modified the stimuli to yield two nonoverlapping stimulus dimensions: large figures with holes inside them (see Figure 1B). The two stimulus dimensions are the shapes of the large figures and the shapes of the holes inside. We made six exemplars for both stimulus dimensions. The areas of the small and large figures were the same, for all exemplars.

In other aspects, the eye-tracker adapted IEDT used in this study was similar to the CANTAB version of the IEDT. Participants took part in a visual discrimination task, where two compound stimuli were presented with distinct stimulus dimensions (in our case a large shape with a hole inside). Subjects were instructed to choose between two stimuli and to figure out the reward contingency based on feedback. We also told them, that after learning the rule, indicated by consecutive correct responses, the rule would be changed. However, this

change was not signaled to them, it could become evident only from the feedback received. The reward contingency changed after six consecutive correct responses.

During the task, participants advanced through nine different stages, after showing the acquisition of the rule with six consecutive correct responses (see Figure 2). If a participant could not produce this in 100 trials, the task was terminated (this differs from the CANTAB task, where the termination criterion is usually set at 50).

Importantly, the pairing of exemplars from two stimulus-dimensions varied randomly during the subsequent trials: a small figure exemplar could appear with a probability of 0.5 on the surface of both large figure exemplars (e.g. in Figure 2, the exemplars of the two stimulus dimensions are differently paired on the stimulus displays of the last two stages). The only constraint was that the same pairing of large and small figure-exemplars could appear no more than five times.

In the first two stages, the first stimulus dimension was introduced: two large figures with no holes inside were presented on the left and the right side of the screen. One of the large figure exemplars was randomly chosen to be rewarded in stage 1. After six consecutive correct responses the reward contingency was reversed. That is, in stage 2, the other large figure exemplar was rewarded. In stage 3 and stage 4, the rewarded large figure exemplar remained the same, but the second stimulus dimension was introduced. First, in stage 3, two small figure exemplars were presented, which did not overlap with the large figure exemplars (i.e., the small figures were presented under the large figures). Then, in stage 4, the small figures were presented in the middle of the large figures, as holes, creating compound stimuli. Another reversal followed in stage 5: the large stimulus-exemplar (that was not rewarded in stage 2-4) became rewarded again. In stage 6 and stage 7, new large and small figures were used, but the rewarded dimension remained the shape of the large figure. This was termed as an *interdimensional shift of attention*, as subjects had to shift their attention to novel

exemplars of the same dimension. One of the large figures was chosen randomly to be rewarded in stage 6, and the other in stage 7. In stage 8 and stage 9, new exemplars of both stimulus-dimensions were introduced. This time, unlike the previous stages, one of the small figures was rewarded in stage 8, and the other small figure was rewarded in stage 9. This required subjects to make an *extradimensional shift of attention*, as attention from one relevant stimulus-dimension had to be transferred to another dimension. The same two exemplars from both stimulus dimensions were used for all participants in each stage.

<insert Figure 2 about here>

Each selection trial had three phases: first, in a pretrial period, participants had to fixate a fixation cross for 2.5 seconds. Then, during the critical choice period, the two compound stimuli were presented on the screen and participants had to indicate which of them is rewarded. The two stimuli remained on the screen until the participant responded by pressing the left or the right mouse-button (corresponding to the left or to the right figure). The response was followed by a blank screen of 0.5 seconds that was followed by a feedback trial of one second. During the feedback trial, the two stimuli remained on the screen and were surrounded with a green or a red line, signaling a correct or an incorrect choice, respectively. The correct and the incorrect choice was also signalized with different voice signals.

Reaction Time Data

In both tasks, we measured the time between the presentation of the item and the choice indicated by pressing the mouse button (for the WCST task, the time of the presentation phase was assessed, i.e. the time until the first mouse click, excluding the response phase).

Eye-Tracking

Both tasks were administered on a personal computer, using the stimulus presentation software Presentation (Neurobehavioral Systems Inc, Albany, CA). We used the SMI RED500 remote eye-tracker system (SensoMotoric Instruments, Teltow, Germany), with binocular eye-tracking. Data sampling frequency was 120 Hz in Study 1, and 500 Hz in Study 2. Participants were sat in a dimly lit room. In Study 1, lighting conditions were the same for all participants, whereas in Study 2, the similarity of background lighting was not controlled. Nevertheless, even here, the lighting conditions remained constant during each recording, thus within-subject comparisons used in our statistical analyses are not affected by this factor.

Gaze data processing. Points of gaze data were scanned for low precision data by computing the root mean square (RMS) of intersample differences during fixations in each pretrial period (Holmqvist et al., 2011). Participants with mean RMS values exceeding the sample mean by 2 standard deviations were excluded (Study 1: $M_{RMS} = 0.09$, $SD_{RMS} = 0.03$, four participants were excluded; Study 2: $M_{RMS} = 0.19$, $SD_{RMS} = 0.07$, seven participants were excluded).

For processing raw gaze data, the Begaze analyzer software was used (SensoMotoric Instruments, Teltow, Germany). First, fixations and saccades in the raw gaze data were identified. Then, we specified those areas of the stimuli, called Areas of Interests (AOIs), which might be of interest for analyzing information processing. Finally, in both tasks, for each AOI and for each trial, we calculated dwell time values: the percentage of trial time during which the participant fixated the given AOI.

In the WCST task (Study 1), four AOIs were defined, one for each target card (see Figure 1C). Dwell time percentage was summed up for these four AOIs, for each trial, separately. We only took into account dwell time values from the presentation period, between the presentation of the stimuli and the mouse click of the participant indicating a decision. Thus, we did not analyze the response phase: here, participants had to indicate

which card they chose using the cursor, and gaze pattern during this phase might be determined by oculomotor coordination related to moving the cursor, which is not in the focus of our investigation.

In the IEDT (Study 2), two AOIs corresponding to the two relevant stimulus dimensions were defined. For the large figures, the distinctive parts of the large figure were selected, whereas the entire surface of the small figures were involved as part of the AOI (see Figure 1D). In all trials, dwell time values for these AOIs were summed, and these summed dwell time values were calculated for the period between stimulus presentation and the response for each trial.

Pupil data processing. Pupil data were processed using MATLAB (MathWorks, Inc., Natick, Massachusetts, United States). To exclude changes in pupil size due to blinks and other artefacts, all data points were removed, which were more than two standard deviations above the mean pupil size in a given trial. Data from the preceding and subsequent 40 msecs were also removed. The missing data points were interpolated. The ratio of interpolated data points has exceeded by no participants the predefined criterion of 30%, thus no exclusion was made. Finally, data were smoothed using the Savitzky-Golay filter (parameters: polynomial order: 2, frame size: 21).

Tonic activity of the noradrenergic system was assessed by measuring pretrial pupil size. Since gaze position might bias the measurement of pupil size (Hayes & Petrov, 2016), participants were asked to maintain their gaze during the pretrial period on a given point (in Study 1 the location of the to-be-matched card; in Study 2 the fixation cross). For each trial, pretrial pupil size was computed by averaging pupil size values during the pretrial phase, lasting from 1500 to 500 msecs preceding the presentation of the stimulus.

Classification of Trials into Different Trial-Types

As we were interested in periods when the reward contingencies changed, we analyzed in both studies the period before and after rule change. Measurement points related to both pretrial pupil size and AOI dwell times were classified and denoted based on their position relative to a rule shift. We use a corresponding labeling throughout the article. For example, the last pupil size or dwell time value measured before a rule shift is labeled using the denotation RS[-1] (RS standing for rule shift), whereas the second pupil size or dwell time value after a rule shift is labelled using the denotation RS[+2]. These trial types are used as the basis of further statistical analysis.

Importantly, the type of the shift influences at which trial the rule shift becomes evident for the participant, and this affects the classification of trials for analyses involving dwell times. For all shifts in the WCST, and in the reversal shifts of the IEDT (before the 2nd, 5th, the 7th, and the 9th stage), the change of the sorting rule is not accompanied by stimulus display changes, only the to-be-chosen stimulus feature becomes different. In such shifts, the first trial associated with a new rule counts as the last trial where participants have not yet received a negative feedback and thus are not aware of any changes in stimulus-reward contingency (RS[-1], see Figure 3, first row).

In contrast, during several rule shifts in the IEDT (before the 3rd, 4th, 6th, 8th stage), the stimulus display changed, and thus the change in the stimulus-reward contingency was immediately evident for the participant. Thus, in these cases, the first trial associated with the new rule counts as the first trial where the participant is aware that the rule has changed (RS[+1], see Figure 3, second row).

Note that the different dependent variables are measured at different time points: pretrial pupil size is measured before a trial, whereas AOI dwell time and RT is measured during the trial, as illustrated in Figure 3. Because pupil size is measured during fixation crosses, and there is always feedback between two measurement points, the above described

distinction between the two-types of rule shifts does not affect the classification of trials for analyses related to pupil size (See Figure 3, third row).

<insert Figure 3 about here>

Statistical Analysis

There are several indices measuring performance on the WCST. For attentional set shifting, the most important indices are perseverative errors and failures to maintain set. The former refers to incorrect choices which would have been correct in the previous stage, whereas the latter refers to incorrect decisions which appear after three or more correct choices. We computed for all participants the relative frequency of these errors (i.e. their proportion to all responses). In the IEDT task, we computed trials to criterion scores for each stage, that is the number of trials needed to complete a stage.

We averaged the values of the dependent variables (pretrial pupil size ,AOI dwell time and RT) for the different trial-types (e.g. RS[-1] or RS[+2]), across all rule shifts, for both tasks. For example, we averaged the values of pretrial pupil size for all RS[-1] trials of the five rule shifts in the WCST, to get an average RS[-1] value. For participants, who did not complete the task (10 participants in Study 1, and three participants in Study 2), these mean values were computed from fewer values. In the case of the IEDT, values from the first two stages (with only one stimulus dimension) were not involved in this calculation, and are not analyzed.

These averaged trial-type values were then used in ANOVAs, to investigate changes in AOI dwell time and pretrial pupil size before and during rule shifts. For both studies, at first we investigated the exploitative phase, which is the sequence of correct choices leading to rule shift. We used a repeated measures ANOVA with trial as an independent factor, and either pretrial pupil size, AOI dwell time or RT, as a dependent variable. In Study 1, for the WCST, the trial factor had 10 levels (levels: RS[-10] to RS[(-1]), whereas in Study 2, for the

IEDT, the trial factor had six levels (levels: RS[-6] to RS[(-1]). The number of factor levels was determined in both tasks by the criterion to rule shift: that is, in these analyses, we involved all the correct choices leading to a rule shift. We predicted that this period would be associated with an increasingly exploitative mode of responding, thus a continuous decrease of pretrial pupil size, AOI dwell time and RT was expected. To demonstrate this, contrast analysis with polynomial contrasts was used, to detect a linear decrease in the values of the dependent variable, along the factor trial.

Second, we analyzed changes in pretrial pupil size and AOI dwell time during rule shifts - we investigated the three trials preceding and following rule shifts. Again, a repeated measures ANOVA was used to verify our hypotheses with trial as the independent factor (levels: RS[-3] to RS[(+3]), and either pretrial pupil size, AOI dwell time, or RT, as dependent variable. Contrast analysis with repeated contrasts were used to compare changes in the dependent variable between trials.

Finally, because the IEDT consists of qualitatively different rule shifts, additional analysis was also performed to compare the change in pretrial pupil size during different rule shifts of IEDT. We conducted a two-way repeated measures ANOVA with rule shift (from the 3rd phase to the 9th phase) and trial (RS[-3] to RS[+3]) as independent variables, and pretrial pupil size, as a dependent variable (three participants who did not pass the 8th stage were excluded from this analysis).

In all repeated measures analysis, violation of the sphericity assumption was checked using the Mauchly's test. If violation of sphericity was detected, p-values were computed by using the Greenhouse-Geisser correction.

Results

Behavioral Data

In Study 1, all but ten participants completed the WCST task (i.e. found the correct sorting principle six times). The mean proportion of perseverative errors, relative to all trials, was $M = 0.06$ ($SD = 0.07$, range: 0-0.32). The mean number of failures to maintain set was $M = 1.39$ ($SD = 2.22$, range: 0-10). The distribution of both variables was highly skewed, indicating either floor or ceiling effect. Table 1 shows the mean number of choices participants needed to pass a specific stage.

In Study 2, all but three participants completed the IEDT. Mean of trials to complete each phase is presented in Table 2. As can be seen, most rule shifts were solved relatively easy, as the mean trials to criterion score exceeded the minimum value of six correct choices only by a small amount. As expected, the only exception was the 8th stage, where higher trials to criterion values indicated that the extradimensional shift is the most difficult phase of the task. This impression was also confirmed by a repeated measures ANOVA with the independent factor of phase (1 to 9), which showed significant differences in trials to criterion scores between the phases, $F(8, 568) = 10.87$, $p < .001$ (Greenhouse-Geisser corrected, epsilon = 0.26), $\eta_p^2 = .14$ (the three participants not passing the 8th stage are not involved). Repeated contrasts also revealed that there was a significant decrease after the 3rd and the 8th phase ($F[1, 71] = 9.68$, $p < .01$, $\eta_p^2 = .12$, and $F[1, 71] = 17.19$, $p < .001$, $\eta_p^2 = .20$, respectively), and a significant increase before the 8th phase ($F[1, 71] = 21.61$, $p < .001$, $\eta_p^2 = .23$). But even in this stage, requiring complex extradimensional shift of attention, there was a highly skewed distribution of trials to criterion (e.g. 59% of the participants only required 12 or less trials to pass the stage), indicating high levels of performance.

<insert Table 1 about here>

<insert Table 2 about here>

Pupil Size Changes During the Trials

Pupil size changes during a trial are presented for the WCST (Study 1) in Figure 4A, and for the IEDT (Study 2) in Figure 4B. As can be seen, there is a steep decrease in pupil size after the presentation of the trials – this might be related to the presentation of new stimuli or to changes in illuminance of the fixated position. For our present purposes, the pretrial period is of more importance. As can be seen, pretrial pupil size is smaller preceding rule shifts than following it, suggesting that rule shift is associated with increased tonic NA activation.

<insert Figure 4 about here>

Study 1, WCST - Exploitative Phase

The ANOVA with trial as an independent factor and pretrial pupil size as a dependent variable resulted in a significant effect of trial, $F(9, 540) = 19.61$, $p < .001$ (after Greenhouse-Geisser correction, epsilon = 0.76), $\eta_p^2 = .25$. Contrast analysis indicated a significant linear trend for the factor trial, $F(1, 60) = 82.06$, $p < .001$, $\eta_p^2 = .58$ (see Figure 5A). Similar pattern emerged for the analyses involving dwell times. We found a significant effect of trial, $F(9, 540) = 1.97$, $p < .05$, $\eta_p^2 = .03$, and again, a significant linear trend for the factor trial, $F(1, 60) = 9.86$, $p < .01$, $\eta_p^2 = .14$ (see Figure 5B). Finally, for RTs, we found a significant main effect of trial, $F(9, 540) = 18.35$, $p < .001$, $\eta_p^2 = .23$ (after Greenhouse-Geisser correction, epsilon = 0.53), and a significant linear trend, $F(1, 60) = 82.30$, $p < .001$, $\eta_p^2 = .58$ (see Figure 5C). In brief, during the exploitative phase, tonic noradrenergic activity, indexed by pupil size, attention towards relevant stimulus-features, indexed by dwell time values, and also RTs decreased linearly, as hypothesized.

Study 1, WCST - Rule Shifts

The ANOVA with pretrial pupil size as a dependent variable and trial as an independent factor showed a significant effect of trial, $F(5, 300) = 26.31$, $p < .001$, $\eta_p^2 = .31$. Repeated contrast analysis suggested that pretrial pupil size significantly increased between

RS[-1] and RS[+1], $F(1, 60) = 14.52$, $p < .001$, $\eta_p^2 = .20$, and also between RS[+1] and RS[+2], $F(1, 61) = 6.71$, $p < .05$, $\eta_p^2 = .10$ (see Figure 5D). Regarding dwell times, the ANOVA showed a significant effect of trial, $F(5, 300) = 6.03$, $p < .001$ (after Greenhouse-Geisser correction, epsilon = 0.82), $\eta_p^2 = .09$. Repeated contrasts indicated a significant increase between RS[-1] and RS[+1], $F(1, 60) = 10.73$, $p < .01$, $\eta_p^2 = .15$ (see Figure 5E). For RTs (see Figure 5F), a significant main effect of trial emerged, $F(5, 300) = 17.67$, $p < .001$, $\eta_p^2 = .23$ (after Greenhouse-Geisser correction, epsilon = 0.53), with significant repeated contrasts between RS[-1] and RS[+1], $F(1, 60) = 32.94$, $p < .001$, $\eta_p^2 = .35$, and between RS[+1] and RS[+2], $F(1, 60) = 5.69$, $p < .01$, $\eta_p^2 = .09$. Thus, in line with our hypothesis, pretrial pupil size, AOI dwell time values and also RTs increased significantly after rule shifts (the increase of pretrial pupil size is also shown on Figure 2A).

<insert Figure 5 about here>

Study 2, IEDT - Exploitative Phase

The ANOVA with trial as an independent variable and pretrial pupil size as a dependent variable showed a significant effect of trial, $F(5, 370) = 45.23$, $p < .001$ (after Greenhouse-Geisser correction, epsilon = 0.85), $\eta_p^2 = .38$. Linear contrasts indicated a linear decrease in the values of pupil size with trials approaching the rule shift, $F(1, 74) = 142.26$, $p < .001$, $\eta_p^2 = .66$ (see Figure 6A). A similar pattern was evident for analysis involving AOI dwell time as dependent variable. The ANOVA with trial as an independent variable showed a significant effect for trial, $F(5, 370) = 14.18$, $p < .001$ (after Greenhouse-Geisser correction, epsilon = 0.87), $\eta_p^2 = .16$. Linear contrast showed that there was a linear decrease in AOI dwell time, when participants proceeded in the exploitative phase from trial to trial, $F(1, 74) = 45.55$, $p < .001$, $\eta_p^2 = .38$ (see Figure 6B). Finally, for RTs, we revealed a significant main effect of trial, $F(5, 370) = 41.57$, $p < .001$, $\eta_p^2 = .36$ (after Greenhouse-Geisser correction, epsilon = 0.50), along with a significant linear trend, $F(1, 74) = 75.17$, $p < .001$, $\eta_p^2 = .50$ (see

Figure 6C). Thus, similarly to Study 1, we found a steady decrease in pretrial pupil size, AOI dwell time, and RTs.

Study 2, IEDT - Rule Shifts

The ANOVA conducted with trial as an independent variable and pretrial pupil size as a dependent variable resulted in a significant effect of trial, $F(5, 370) = 60.97$, $p < .001$ (after Greenhouse-Geisser correction, epsilon = 0.71), $\eta_p^2 = .45$ (see Figure 6D). Contrast analysis revealed significant differences between RS[-1] vs RS[+1], $F(1, 74) = 192.01$, $p < .001$, $\eta_p^2 = .72$, between RS[+1] vs RS[+2], $F(1, 74) = 49.40$, $p < .001$, $\eta_p^2 = .40$ and also between RS[+2] vs RS[+3], $F(1, 74) = 14.25$, $p < .001$, $\eta_p^2 = .16$. To analyze effects related to dwell times, an ANOVA with trial as an independent variable was run. We found a significant effect of trial, $F(5, 370) = 26.18$, $p < .001$, $\eta_p^2 = .26$ (see Figure 6E). Contrast analysis revealed significant differences between RS[-1] vs RS[+1], $F(1, 74) = 78.75$, $p < .001$, $\eta_p^2 = .52$ and RS[+1] vs RS[+2], $F(1, 74) = 35.71$, $p < .001$, $\eta_p^2 = .33$. Similarly, we found a significant main effect of trial on RTs, $F(5, 370) = 94.98$, $p < .001$, $\eta_p^2 = .56$ (after Greenhouse-Geisser correction, epsilon = 0.37), and contrast analysis indicated significant differences between RS[-1] vs RS[+1], $F(1, 74) = 135.46$, $p < .001$, $\eta_p^2 = .65$ and RS[+1] vs RS[+2], $F(1, 74) = 96.62$, $p < .001$, $\eta_p^2 = .57$ (see Figure 6F). Thus, again, we showed that AOI dwell time, pretrial pupil size and RTs increased after rule shifts (see also Figure 2B).

<insert Figure 6 about here>

Study 2, IEDT - Analysis of Different Shift Types

A repeated measures ANOVA with rule-shift and trial as independent variables and pretrial pupil size as a dependent variable was run. The results showed a significant main effect of trial, $F(5, 355) = 46.15$, $p < .001$ (after Greenhouse-Geisser correction, epsilon = 0.75), $\eta_p^2 = .39$, a significant main effect of rule shift, $F(5, 355) = 2.67$, $p < .05$ (after Greenhouse-Geisser correction, epsilon = 0.76), $\eta_p^2 = .04$, and also a significant rule shift x

trial interaction, $F(25, 1775) = 3.25$, $p < .001$ (after Greenhouse-Geisser correction, epsilon = 0.58), $\eta_p^2 = .04$. This latter interaction indicates that the change of pupil size is different for the different shifts. This is also justified by the visual inspection of Figure 7, where the change of pupil size is presented for the different phases. In all shifts, except for the extradimensional shifts, the steep increase of pretrial pupil size after rule shift is followed by a decrease during the following two trials. In contrast, in the case of the extradimensional shift (highlighted with red color), the pretrial pupil size does not decrease during the first three trials. This impression is validated using a series of ANOVAs, with the trials preceding and following the different rule shift (RS[-3] to RS[+3], as independent variables, and pretrial pupil size as dependent variables. The results are presented in Table 3. The main effect of trial was significant for all ANOVAs (all Fs > 3, all ps < .01), as were the repeated contrasts comparing pretrial pupil size values immediately before and after the rule shift (RS[-1] vs.RS[+1]), indicating the increase of pretrial pupil size after rule shift. Crucially, the repeated contrast comparing pretrial pupil size values between RS[+1] and RS[+2] indicated significant decrement of pupil size for all shifts, except the extradimensional shift. This indicates that unlike by other shifts, pretrial pupil size does not decrease in a short time after the extradimensional shift.

<insert Figure 7 about here>

<insert Table 3 about here>

Discussion

In both studies, we found evidence that attentional set shifting is related to NA transmission and to increase in tonic LC firing: rule shifts were related to an increase in pretrial, baseline pupil diameter. After rule shifts, the previously learnt stimulus-reward contingencies were not valid anymore, which necessitated the exploration of the situation through trial and error behavior. Our findings provide evidence that LC/NA system activity

underlies such explorative behavior: the LC/NA system shifts to a more explorative state, which is associated with higher tonic level firing of the LC, and this is then reflected in baseline pupil size. Moreover, our results also suggest that the pretrial pupil size signals changes in the exploration-exploitation trade-off. During the sequence of correct choices leading to rule changes, we found a gradual decrease in pretrial pupil size, which can be interpreted as a gradual shift from explorative to exploitative behavior. These results are also confirmed by analyzing attentional patterns during the task: there was a gradual decrease in dwell times on the stimuli during the correct trials leading to rule shifts, whereas trials after rule shifts were characterized by an increased dwell time on the stimuli. Finally, the pattern of RT changes mirrored changes of pretrial pupil size and dwell time percentage: steady decrease before rule shifts, followed by a sharp increase after the shift.

These basic findings were similar in both the WCST and the IEDT, suggesting that such tonic changes are essential for attentional set shifting, regardless of the specific task features. Nevertheless, attentional set shifting is a complex process. In the WCST, the different components of attentional set shifting are hard to disentangle, thus we focused on the IEDT in discussing which process might be related to tonic NA. Our analysis showed that increase in tonic NA activity was present regardless of the type of the rule shift. Pretrial pupil size was also increased by simple reversal learning and also by the more complex intra- or extradimensional set shifting. In the former case, the stimulus display was constant, and negative feedback signaled that the stimulus-reward contingencies changed. In the latter case, a pronounced change of the stimulus-display signaled the change of stimulus-reward contingencies before any feedback was given to the participant. Thus, heightened tonic activity of the NA system is not a specific characteristic of attentional set shifting, and is not related to feedback or stimulus-changes per se, but is provoked if any change in stimulus-

reward contingencies is detected. This is in accordance with the account of Yu and Dayan (2005), who suggested that tonic NA is related to unexpected uncertainty.

Our results also suggest that the increase in tonic NA activity is more than a simple arousal response provoked by an unexpected change in the environment. During the extradimensional shift, unlike any other shifts, the size of the pupil did not start to decrease on the 2nd and 3rd trial after the shift. This might be explained by the fact, that in this stage, participants needed more trials to find out that the relevant stimulus dimension has changed, and until then, explorative behavior was required. Similarly, analysis involving the exploitative phase also suggest, that tonic activity starts to decrease only after the new stimulus-reward contingencies are found. Thus, in accordance with the adaptive gain theory (Ashton-Jones & Cohen, 2005), this pattern of results suggest that the heightened tonic activity is maintained until the new stimulus-reward contingencies are found, and an exploitative phase of behavior can start.

When interpreting our results, some limitations must also be considered. First, although several lines of research suggest that pupil size is correlated with LC firing rates, the origin of this correlation is not revealed, and is most probably a result of a common background factor (Joshi et al., 2015). This necessitates some caution when interpreting our results, and further research should clarify the causal pathways relating NA transmission and attentional set shifting.

Second, the complex visual stimuli used in our studies did not permit to measure phasic response during the active viewing of the stimuli (both luminance levels and gaze location would have introduced unacceptable levels of noise). Thus, exploitative phase was defined only indirectly, based on task-features and the decrement in tonic pupil size. Further research should strengthen our conclusions by measuring both tonic and phasic response of the pupil.

Third, an alternative explanation of our results is possible: the adaptive gain theory proposes a curvilinear relationship between LC activity and task performance (Ashton-Jones & Cohen, 2005; Hopstaken, van der Linden, Bakker, & Kompier, 2015a, 2015b): low tonic LC activity is associated with drowsiness/inattentiveness (poor task performance), middle levels with exploitation (appropriate task performance), and high levels with exploration (poor task performance). Consequently, during preshift trials, when the task contingencies are known to the participants and the task is relatively easy, the small pupil size might signal mental boredom/low arousal/fatigue (and not exploitation). Accordingly, the increase in pupil size after the change in stimulus-reward contingency might be related to a shift to exploitation (and not to exploration). In accordance with this idea, mental fatigue, inattentiveness and mindwandering are often associated with small pupil dilation (Hopstaken et al., 2015a, 2015b; van den Brink, Murphy, Nieuwenhuis, 2016; Unsworth & Robison, 2015,2016). Note however, that in the above studies, mental fatigue is also associated with erratic performance (Hopstaken et al., 2015a, 2015b) mindwandering (Unsworth & Robison, 2016) and slow reaction times (van den Brink et al., 2016; Unsworth & Robison, 2015). In contrast, in our study, the decrease of pupil size was associated with errorless performance and a speed up of reaction times. Because of this, we suggest that the preshift phase in our study is not characterized by mental fatigue or boredom. Further research investigating phasic responses during attentional set shifting might be decisive on this issue, because high phasic LC would differentiate between exploitation and exploration (Ashton-Jones & Cohen, 2005; Hopstaken et al., 2015a, 2015b).

These limitations notwithstanding, our results confirm that the LC/NA system regulates the amount of exploration, and as a result, underlies cognitive flexibility. Considering that attentional set shifting is suggested to be an endophenotype or a cognitive marker for several psychiatric and neurological conditions (e.g. Chamberlain et al, 2006;

Owen et al., 1993), this evidence might be relevant for translational research aiming to delineate the neurobiological and genetic background of different psychiatric and neurological conditions. Furthermore, the result that tonic NA levels are related to explorative attentional processes, could prove that theories about the functions of LC activity, mainly based on animal research, are valid for humans as well. Finally, the tonic increase in LC firing levels was associated with both simple reversal learning and complex attentional set shifting. Consequently, tonic increase in LC firing might be triggered by any situation where stimulus-reward contingencies change, and new ways of behavior are required. Thus, our results are not only informative regarding the neuronal background of attentional set shifting, but also confirm the basic role of LC/NA system in behavior control.

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Conflict of interest

The authors declare no conflict of interest.

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Table 1.

Performance on the Wisconsin Card Sorting Task in Study 1

Measures	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6
Trials to criterion	18.66 (12.93)	20.14 (15.25)	15.29 (8.25)	15.42 (6.08)	13.50 (3.63)	13.56 (6.89)
Pass%	97%	90%	90%	89%	85%	85%

Notes. Trials to criterion: number of trials (choices) required to complete a stage (values represent mean values, standard deviations are shown in parentheses). Pass%: percentage of participants successfully completing a stage.

Table 2.

Performance on the Intra/Extradimensional Set Shifting Task in Study 2

Measures	Stage 1 (SD)	Stage 2 (SDR)	Stage 3 (CD1)	Stage 4 (CD2)	Stage 5 (CDR)	Stage 6 (ID)	Stage 7 (IDR)	Stage 8 (ED)	Stage 9 (EDR)
Trials to criterion	7.57 (2.74)	8.29 (3.48)	9.60 (4.99)	7.67 (3.45)	8.08 (1.86)	7.57 (3.25)	8.55 (3.63)	19.16 (21.01)	10.85 (13.93)
Pass%	100%	100%	100%	100%	100%	100%	100%	96%	95%

Notes. Trials to criterion: number of trials/choices required to complete a stage (values represent mean values, standard deviations are shown in parentheses); Pass%: percentage of participants successfully completing a stage; SD: Simple Discrimination; SDR: Simple Discrimination Reversal; CD1: Compound Discrimination 1; CD2: Compound Discrimination 2; CDR: Compound Discrimination Reversal; ID: Intradimensional Set Shifting; IDR: Intradimensional Set Shifting Reversal; ED: Extradimensional Set Shifting; EDR: Extradimensional Set Shifting Reversal.

Table 3.

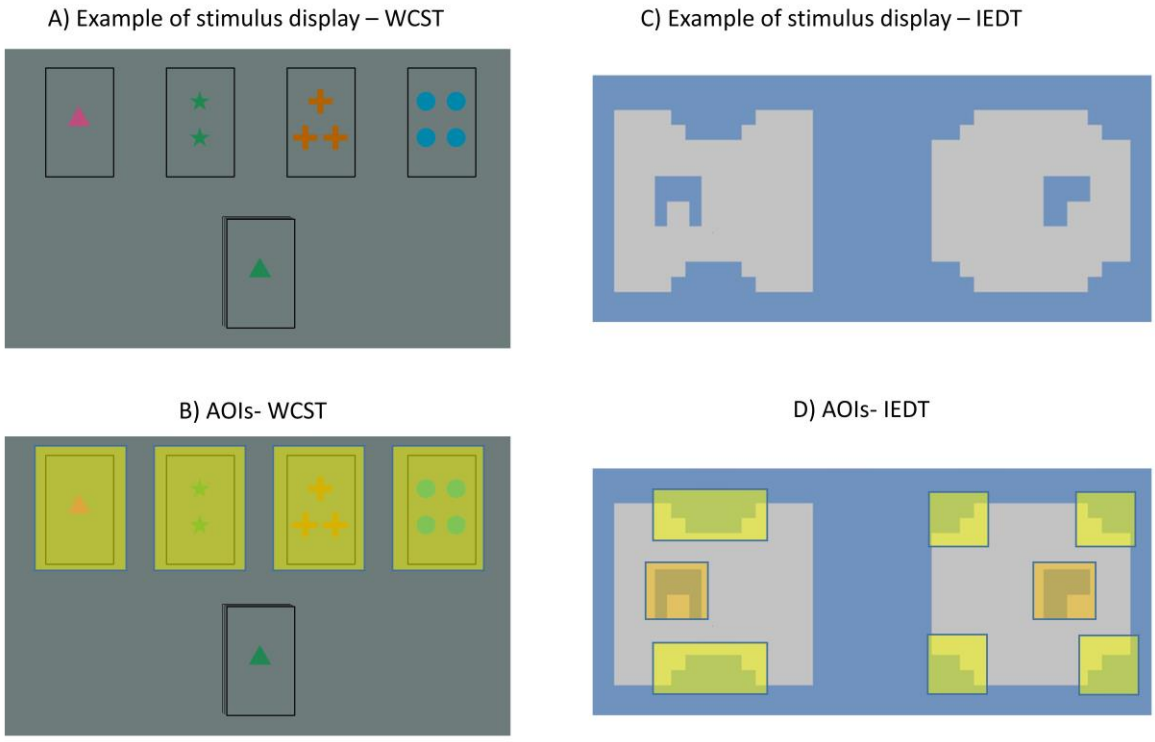
Results of ANOVAs, Conducted Separately for the Different Rule Shifts of the IEDT

Rule shift	F-test	Contrast analysis (repeated contrast)		
		RS[-1] vs RS[+1]	RS[+1] vs RS[+2]	RS[+2] vs RS[+3]
CD1-CD2	F=3.7**	F=14.9***	F=10.2***	F=0.5
CD2-CDR	F=24.5***	F=70.3***	F=22.7***	F=15.6***
CDR-ID	F=14.7***	F=55.6***	F=14.9***	F=2.3
ID-IDR	F=10.8***	F=32.0***	F=26.8***	$F=3.7^{+}$
IDR-ED	F=12.7***	F=35.3***	F=0.2	F=1.5
ED-EDR	F=10.1***	F=45.2***	F=6.6*	F=9.8**

Notes. Repeated measures ANOVAs. For each shift, pretrial pupil size values from the three trials preceding and following rule shifts are involved in the analysis. For all analyses, the Greenhouse-Geisser Correction was used for calculating p-values, epsilon values ranged from .74 to .86, η_p^2 values ranged from .05 to .25. RS[-1]: trial preceding the rule shift; RS[+1], RS[+2], RS[+3]: the first, second or third trial, respectively, following the rule shift. CD1: Compound Discrimination 1; CD2: Compound Discrimination 2; CDR: Compound Discrimination Reversal; ID: Intradimensional Set Shifting; IDR: Intradimensional Set Shifting Reversal; ED: Extradimensional Set Shifting; EDR: Extradimensional Set Shifting Reversal. * $p < .05$; ** $p < .01$; *** $p < .001$, $^{+}$ $p < .10$.

Figure 1.

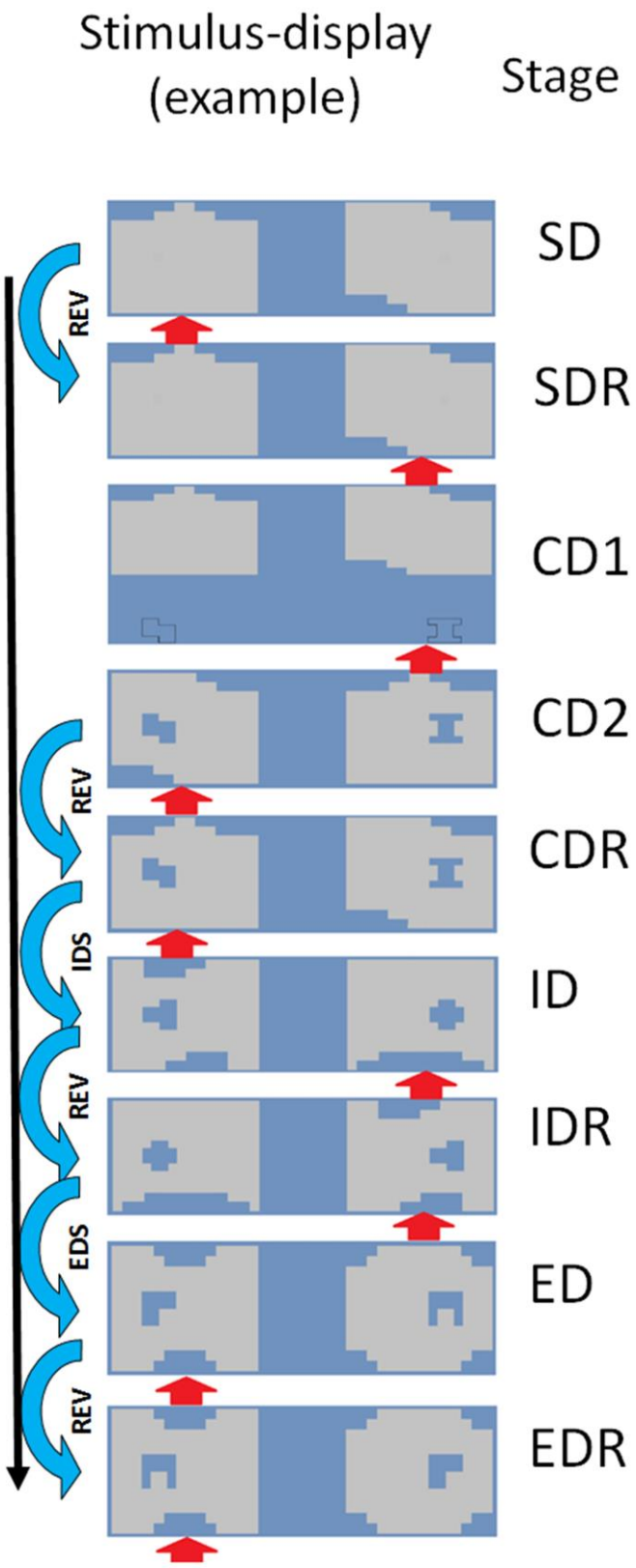
Stimulus Display and Area of Interests Used in Study 1 and Study 2



Notes. (A) Example for the stimulus display in the Wisconsin Card Sorting Task (WCST, Study 1), consisting of four target cards in the upper part of the screen, and a to-be-matched card at the bottom; (B) the four target cards are designated as Area of Interests (AOIs); (C) an example for the stimulus display in the Intra/Extradimensional Set Shifting Task (IEDT, Study 2) adapted for eye-tracking; (D) The relevant parts of the two stimulus dimensions (large shapes vs. small shapes inside) are spatially distinct, thus different AOIs can be designated to them.

Figure 2.

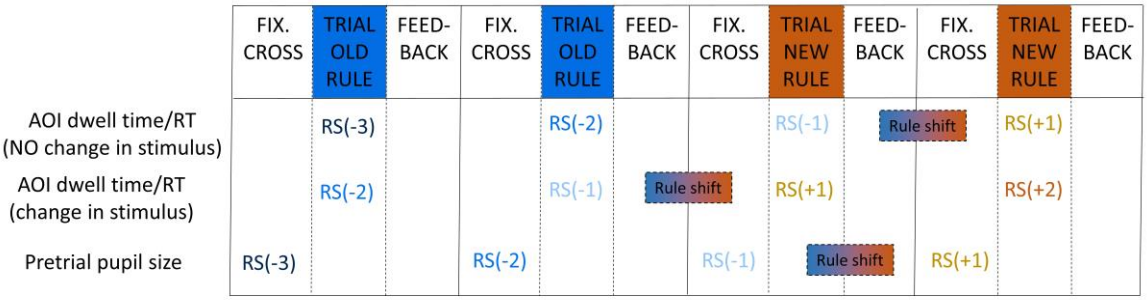
Structure of the Intra/Extradimensional Set Shifting Task, Used in Study 2



Notes. Example of possible stimulus displays and reward-stimuli contingencies are presented. The two stimulus dimensions are the form of the large and small shapes. Each figure represents one trial from the given stage. The exemplars of the two dimensions are paired with each other randomly in each trial (see. e.g. the two exemplars of the 8th and the 9th stage). The red arrow represents the rewarded compound stimulus. In the first two stages, the first stimulus dimension (large shapes) is introduced, followed by the introduction of the second stimulus dimension (small shapes) between the third and the fifth stage. New stimulus exemplars are introduced after the fifth and the seventh stage. During the first seven stages, one of the large shapes is rewarded, whereas in the last two stages, one of the small shapes is rewarded. SD: Simple Discrimination; SDR: Simple Discrimination Reversal; CD1: Compound Discrimination 1; CD2: Compound Discrimination 2; CDR: Compound Discrimination Reversal; ID: Intradimensional Set Shifting; IDR: Intradimensional Set Shifting Reversal; ED: Extradimensional Set Shifting; EDR: Extradimensional Set Shifting Reversal; REV: reversal; IDS: Intradimensional Attentional Set Shift; EDS: Extradimensional Attentional Set Shift.

Figure 3.

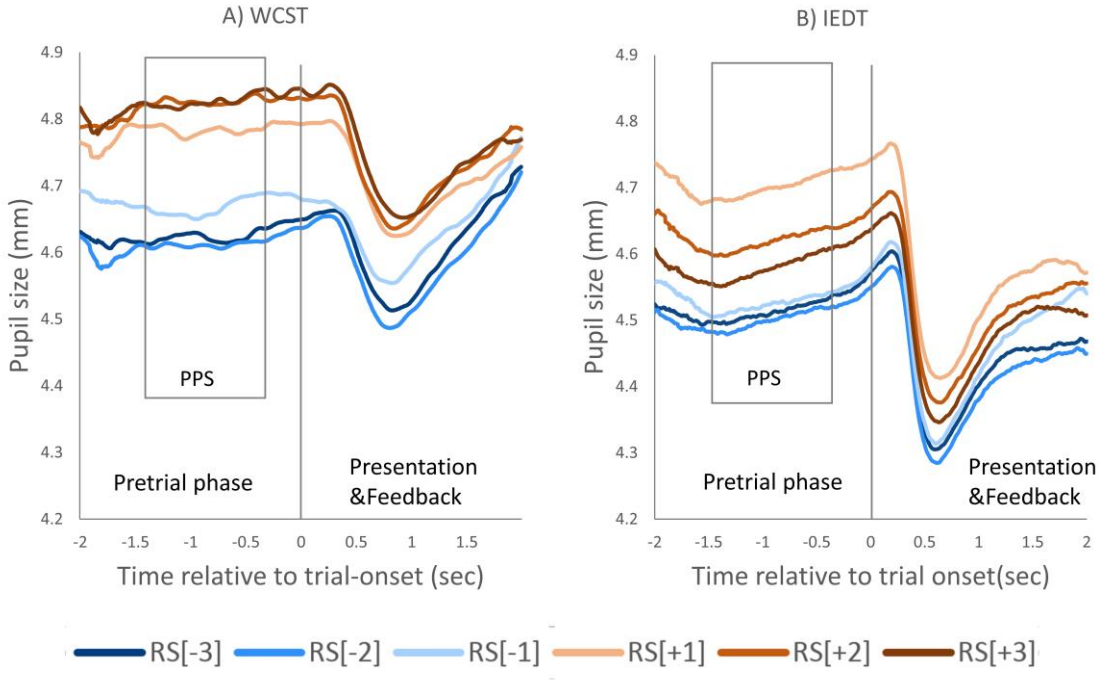
Classification of Trials Depending on the Relative Position to Rule Shifts



Notes. For computing AOI dwell time (AOI-DT) or reaction time (RT) values for the first trial after a shift, different trials should be taken in account, dependent on the type of the rule shift. If there is no change in stimulus display (first row), the rule shift will be evident for the participant only after the first negative feedback. In these cases, only the subsequent trial will be categorized as the first trial following a rule shift (RS[+1]). In contrast, if there is a change in stimulus display during the presentation of a trial (second row), then a change in stimulus-reward contingencies should be evident immediately, thus this trial will be categorized as RS[+1]. This distinction is not relevant for values of pretrial pupil size (PPS), because it is measured before each trial (third row). RS[-1], RS[-2], RS[-3]: the first, second or third trial, respectively, preceding the rule shift; RS[+1], RS[+2]: the first, second or third trial, respectively, following the rule shift.

Figure 4.

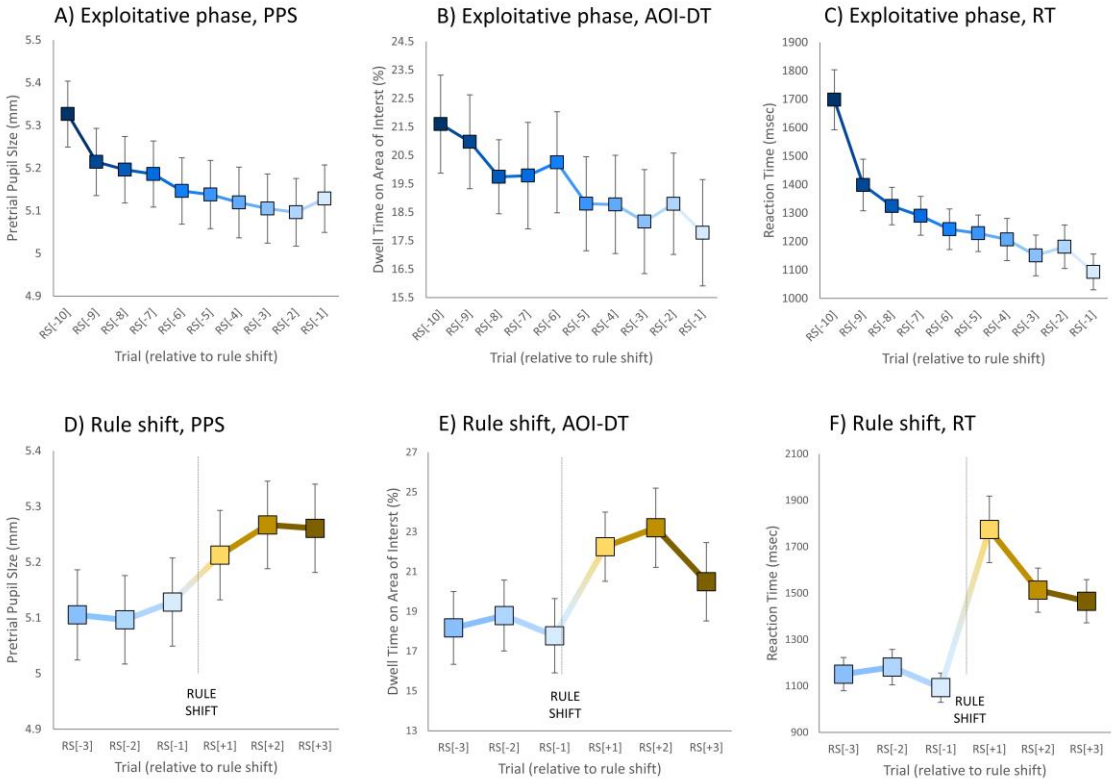
Changes in Pupil Size During the Pretrial, the Presentation and the Feedback Phase



Notes. Grand average of pupil size is depicted, averaged across all rule shifts, for both the Wisconsin Card Sorting Task (A) and the Intra/Extradimensional Set Shifting Task (B). PPS: pretrial pupil size; RS[-1], RS[-2], RS[-3]: the first, second or third trial, respectively, preceding the rule shift; RS[+1], RS[+2], RS[+3]: the first, second or third trial, respectively, following the rule shift.

Figure 5.

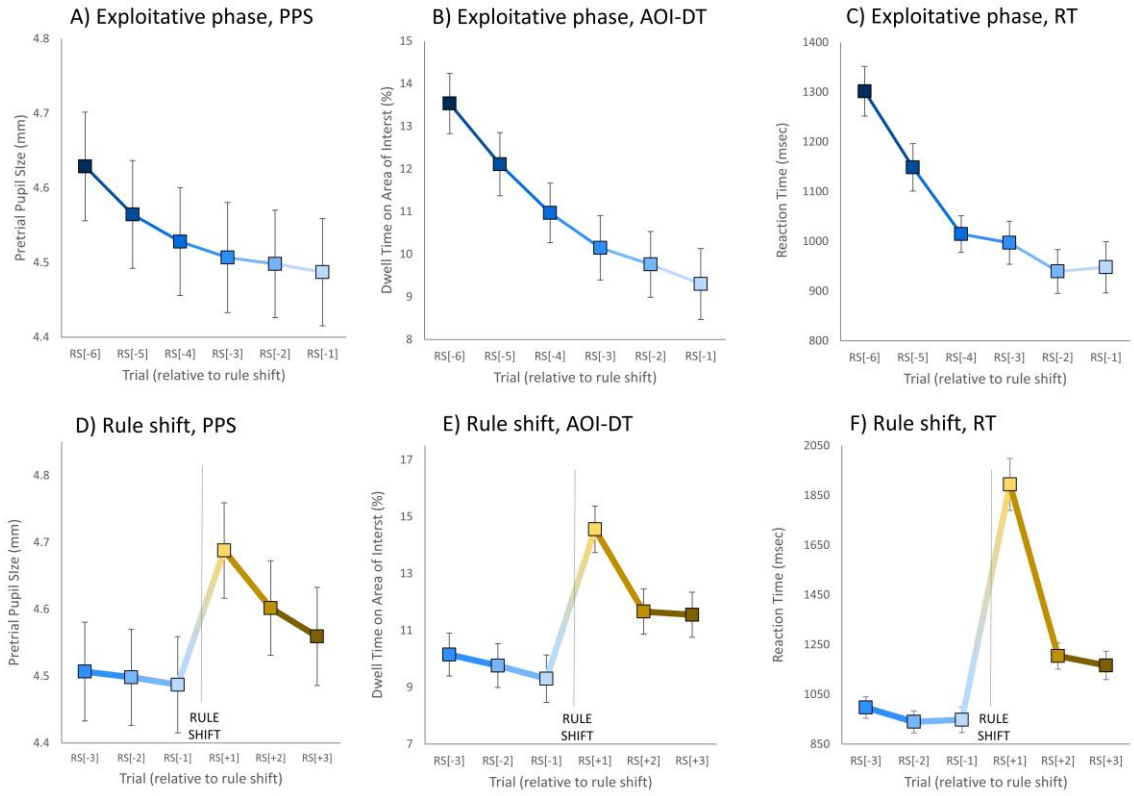
Changes in Pretrial Pupil Size, Gaze Patterns and RTs in the Wisconsin Card Sorting Task, Related to the Exploration-Exploitation Trade-off (Study 1)



Notes. Data points represent mean values averaged across the different rule shifts of the Wisconsin Card Sorting Task. PPS: pretrial pupil size; AOI-DT: Area of Interest – Dwell Times; RT: Reaction time; RS[-1], RS[-2], RS[-3]: the first, second or third trial, respectively, preceding the rule shift; RS[+1], RS[+2], RS[+3]: the first, second or third trial, respectively, following the rule shift. Error bars represent the standard error of the mean.

Figure 6.

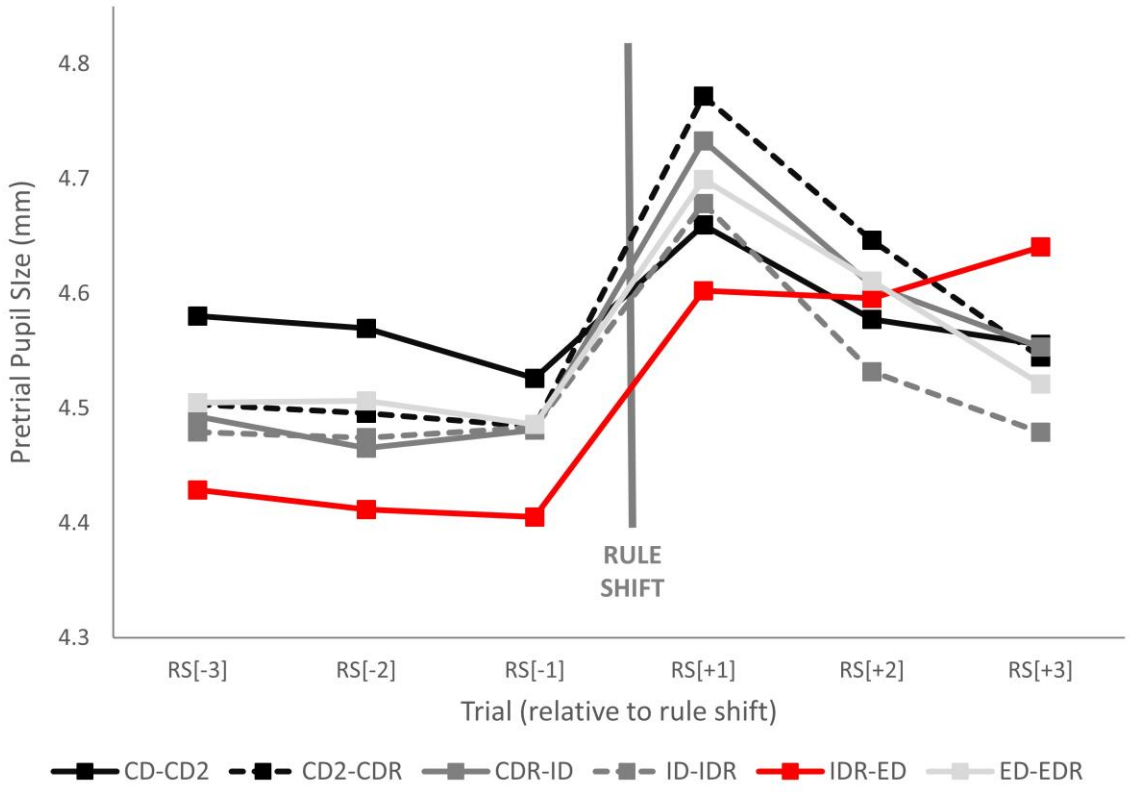
Changes in Pretrial Pupil Size, Gaze Patterns and RTs in the Intra/Extradimensional Set Shifting Task, Related to the Exploration-Exploitation Trade-off (Study 2)



Notes. Data points represent mean values averaged across the different rule shifts of the task. PPS: pretrial pupil size; AOI-DT: Area of Interest – Dwell Times; RT: Reaction time; RS[-1], RS[-2], RS[-3]: the first, second or third trial, respectively, preceding the rule shift; RS[+1], RS[+2], RS[+3]: the first, second or third trial, respectively, following the rule shift. Error bars represent the standard error of the mean.

Figure 7.

Change of Pretrial Pupil Size After Rule Shifts Between Different Phases of the Intra/Extradimensional Set Shifting Task (Study 2)



Notes. Data points represent mean values of pretrial pupil size, averaged separately for shifts between different stages of the task. RS[-1], RS[-2], RS[-3]: the first, second or third trial, respectively, preceding the rule shift; RS[+1], RS[+2], RS[+3] the first, second or third trial, respectively, following the rule shift; CD1: Compound Discrimination 1; CD2: Compound Discrimination 2; CDR: Compound Discrimination Reversal; ID: Intradimensional Set Shifting; IDR: Intradimensional Set Shifting Reversal; ED: Extradimensional Set Shifting; EDR: Extradimensional Set Shifting Reversal.