Analysis of the Effects of Psychotropic Medication on the Behavior of Individuals Diagnosed with Autism

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by
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Abstract

A variety of psychotropic medications are used to decrease problem behavior in children and adults with autism-spectrum disorders. Although some research indicates that medication can differentially affect topographies of behavior with differing response classes, there is limited research that presents systematic data on the specific behavior-altering effects of these drugs. In the present study, we examined the relations between doses of psychotropic medication and levels of a number of different topographies of behavior. Findings are discussed as a step toward a data-driven method of prescribing, titrating, and tapering psychotropic medication.
Analysis of the Effects of Psychotropic Medication on the Behavior of Individuals Diagnosed with Autism

Individuals diagnosed with a developmental disability often exhibit challenging behaviors such as aggression, stereotypic behavior, and self-injurious behavior (SIB) (Iwata & Rodgers, 1992; Luiselli, Matson & Singh, 1991). These behaviors can lead to institutionalism, restraint, decreased independence, and an overall poor quality of life.

A variety of psychotropic medications are used as treatment for problem behavior in individuals with autism. Reviews have found the prevalence for the use of psychotropic medication within this population to be as high as 46% (Langworthy-Lam et al., 2002; Oswald & Sonenklar, 2010; Symons et al., 2002); within institutional settings up to 75% of individuals were prescribed a psychotropic agent (Aman & Singh, 1986).

Matson et al. (2000) found that prescription of psychotropic medication within this population is often not empirically supported resulting in individuals being medicated unnecessarily. Although psychotropic drugs may have an inhibitory effect on aberrant behavior (Aman et al., 2002; Handen et al., 2005; Singh & Millichamp, 1986) they also may reduce desirable behaviors (Reis & Aman, 1998; Williams & Saunders, 1998). Individuals with developmental delays already have deficits in necessary skills so the reduction of appropriate behaviors could be significant. In addition to decreasing appropriate behaviors pharmacological drugs can have hazardous side effects (Hellings et al., 2006).

Currently there have been few published studies evaluating the effects of medication using the direct measurement of behavior (Aman & Madrid, 1999; Matson et al., 2003; Singh et al., 2005). In fact, in approving risperidone for treating irritability in
children with autism, the FDA referred to studies that relied on indirect data 
(McCracken et al., 2004; Shea et al., 2002).

Researchers have used direct observation of behavior when evaluated the effects 
of a variety of medications, including naltrexone for treating self-injury (Thompson et 
al., 1994), methylphenidate in the context of functional analysis sessions (Northrup et 
al., 1997a,b, 1999), and risperidone for treating aggression, self-injury and 
environmental destruction (Dartnall et al., 1999; Valdovinos et al., 2002).

Valdovinos et al. (2002) evaluated medication effects on problem behavior using 
direct measurement and indirect assessment methods. The experimenters evaluated the 
effects of risperidone on problem behavior for two adults with developmental 
disabilities using different methods of direct assessment across medication and placebo 
phases. Direct observation included the collection of daily data by direct care staff using 
15-min partial-interval recording, 30 min time sample collected by the experimenter 
three to four times per week. Weekly functional analysis sessions were also conducted 
to further analyze the medication effects. The experimenters conducted the indirect 
assessment by asking the behavior specialist and direct care staff to complete a 
questionnaire. IOA was collected for the experimenter observations and the functional 
analyses sessions but was not reported for the daily data.

The daily data collected by the direct care staff indicated that risperidone may 
have decreased problem behavior and the functional analysis sessions showed elevated 
rates of responding in the placebo and taper phases. However, no treatment effect was 
observed in the experimenter sample observation sessions. This leads to the question as 
to whether the observation was too small to capture the effects of the medication, or
whether the data the staff collected were not reliable. Results from the rating scales indicated that risperidone did have a suppressive effect, although the researchers reported disagreements regarding the most effective dose.

Direct measurement of the effects of medication involves defining the target behavior and creating a measurement system based on frequency or duration (Zarcone, Napolitano, & Valdovinos, 2008). Some studies have included multiple topographies of behavior within the definition of the dependent variable. Problem behavior is generally used to denote multiple topographies of behavior that may or not belong to the same response class (Borrero & Borrero, 2008; Romaniuk et al., 2002; Worsdell et al., 2000). For example, Northrup et al. (1997) examined the effects of methylphenidate on the disruptive behavior of a child with ADHD. Disruptive behavior included inappropriate vocalizations, out-of-seat behavior, and inappropriate play behavior.

Categorizing multiple responses together as one dependent label may threaten the internal validity of an assessment or treatment. Complications may arise in assessment if multiple topographies of the dependent variable are members of separate operant classes. For example, if one or more topographies of problem are maintained by automatic reinforcement, behavior may occur in all functional analysis conditions, yielding inconclusive results (Vollmer, Marcus, & LeBlanc, 1994).

After analyzing inconclusive functional analysis results Thompson et al. (1998) conducted a second functional analysis and found that different topographies of aggression emitted by a young boy with Pervasive Developmental Disorder (PDD) had separate operant functions. Chin grinding was insensitive to social contingencies while hitting and kicking were maintained by attention.
There is evidence that medication may have differential effects on response classes and topographies. Crosland et al. (2003) conducted a functional analysis of destructive behavior for two adults with developmental disabilities while on and off of risperidone. For both participants the medication decreased responding in the demand condition but did not affect behavior maintained by access to tangible items and attention. Differential effects on self-injurious behavior (SIB) versus aggression were observed for one participant.

Measuring the direct effects of medication on specific topographies of behavior provides a comprehensive analysis that may guide systematic evaluation of psychotropic prescription. In attempt to extend the literature on the measurement of medication effects, the purpose of the present study was to evaluate the effects of psychotropic medication across a range of doses and across different topographies of problem behavior.

**Method**

**Participants and Setting**

All participants attended a residential school for children with autism. Bill and Steve were in staff-intensive unit of the school because of the severity of their problem behavior. All medication prescribed for treatment was in conjunction with behavioral treatment. It had been previously demonstrated function based assessment and treatment alone were not successful in decreasing the target behaviors to acceptable rates. Bill was 15 years old, Steve was 13 years old and Sarah was 14 years old. All were diagnosed with an Autism Spectrum Disorder; Sarah had an additional diagnosis of bipolar disorder.
Data were collected at the participants’ school and at their residential homes. The daily data collected by staff were collected across the day between the hours of 8 AM and 8 PM. Data were collected during a variety of activities, including leisure periods, meals, community outings, and academic sessions.

**Dependent Variables**

The dependent variables measured were the topographies of problem behavior that were specifically targeted by the medication. In some cases, target behaviors were not separated by topography because the definitions were previously in place and relevant to the student’s individualized education plan (IEP). Bill’s problem behavior included head-directed self-injury, self-biting, aggression and crying. Head-directed self-injury was defined as any forceful contact of Bill’s head to an object from a distance of 6 inches or greater. Self-biting was defined as any instance of Bill’s finger, hand, or arm coming in contact with his teeth. Aggression was defined as any instance of one or two handed grabs, hits or bites. Crying was defined as any instance of crying accompanied by tears. Steve’s problem behavior included self-injury and environmental destruction. Self-injury was defined as forceful physical contact generated from one body part to another. This was generally in the form of his hand coming into contact with his body. Environmental destruction included destruction of property.

Sarah’s problem behavior included self-injury and perseverative behavior. Her perseverative behavior included verbal perseveration and ritualistic behavior. Verbal perseveration was defined as Sarah saying “no” and then repeating what her teacher had previously said. Ritualistic behavior was defined as Sarah prompting her teacher to touch something that her teacher had previously touched. Self-injury was defined as any
instance of Sarah hitting her head against a stationary object, hitting her head with an open hand or closed fist, or pinching, scratching, biting, or hair-pulling herself.

IOA was collected by an independent observer for 34% of sessions averaged across all participants. Agreement was calculated by dividing agreements over total agreements plus disagreements. Average agreement across all responses and participants was 92%.

**Procedure**

*Indirect measurement.*

Indirect measurement was gathered by direct care staff interviews administered by the experimenter. Staff were asked to independently complete a survey that was handed out during their team meeting. The interviews were kept anonymous by having the completed questionnaires were placed in a manila envelope. The staff reporting included the participant’s teachers who were required to have known the student through the duration of the medication taper or titration. The interview was collected at the conclusion of the participant’s medication change. A total of 63 staff participated. The surveys required the staff to answer yes or no to whether the medication had a treatment effect upon the specified behavior.

*Direct measurement.*

Direct measurement data were analyzed in terms of response frequency across time and medication phases. Data under each dose were also aggregated to generate dose response curves. These depicted one data point for each dose of medication that represented the mean number of responses emitted by the participant while on the specified dose of medication.
Daily data. Direct observation data were collected 7 days a week during the hours between 8 AM and 8 PM by the direct care staff. Occurrences of the target behavior were reported as frequency per hour.

Session data. The purpose of session data was to collect interobserver agreement data. These were included as part of the daily data and represented a sample representative of the daily. Session data were obtained by collecting the staff data across ten specified hours throughout the week. Each session was one hour. Observation sessions remained the same throughout the study for each participant. Sessions were observed both at the school and the participant’s residential home.

Conditions

For each participant, target responses were examined across different medication doses during the prescribed taper or titration by the student’s consulting psychiatrist.

Bill’s medication (Abilify) was tapered from 18 mg to 12 mg, decreasing by 2 mg every two weeks. Steve’s medication (Abilify) was increased from 21 mg to 25 mg, increasing by 1 mg every two weeks. Sarah’s medication (Luvox) was discontinued starting from 250 mg and decreasing by 50 mg every 2 weeks.

Results

Figure 1 depicts the results of the indirect analysis of Abilify on Bill’s problem behavior. The majority of the staff interviewed reported that Abilify had a treatment effect on head-directed SIB and self-biting and did not have a treatment effect on crying or aggression.
Figure 2 depicts an example of a graph depicting frequency of responses across time and medication doses (i.e., Bill’s head-directed SIB across decreasing doses of Abilify). Bill did not exhibit SIB during the 18 mg or 16 mg doses. However, Bill’s SIB increased towards the end of the 14 mg phase and maintained at high levels during the 12mg phase. Similar graphs were generated for the purposes of visual inspection for target response but are not depicted.

Figure 3 depicts Bill’s daily data aggregated into dose-response curves. The upper right panel shows the mean number of instances aggression across doses of Abilify. Head-directed SIB is depicted in the top left panel, self-biting in the bottom left panel and crying in the bottom right. As successive dose increases, decreases in aggression, head-directed SIB and crying were observed with but adversely increases in self-biting were observed.

Figure 4 depicts dose response curves representing the average responses per session across each medication phase for Bill. Consistent with Bill’s daily data, decreases were observed in head-directed SIB and aggression, but not in self-biting. In addition, decreases in Bill’s crying were not observed as reflected in his daily data.

For Steve’s indirect assessment, all respondents reported that Abilify had no treatment effect on his SIB or environmental destruction. Therefore, a figure depicting data from his indirect assessment is not included. Figure 5 depicts Steve’s daily data and Figure 6 depicts the session data. The upper panels of the figures depict rate of SIB across medication phases, and the lower panels depict mean environmental destruction across medication phases. Steve’s daily data and session data show decreases across doses for SIB, but not for environmental destruction.
Figure 7 depicts the indirect analyses of the effects of Luvox on Sarah’s problem behavior. The majority of the staff reported that Luvox had a treatment effect for Sarah’s SIB, but not for her ritualistic and perseverative behavior.

Figure 8 depicts daily data for Sarah’s SIB (top panel), verbal perseverance (bottom left panel) and ritualistic behavior (bottom right panel). Although Luvox produced a decrease in Sarah’s SIB, it did not produce decreases in her verbal perseverance or ritualistic behavior. Figure 9 depicts the session data for Sarah’s SIB (top panel), verbal perseverance (bottom left panel) and ritualistic behavior (bottom right panel). The session data show a decrease in all forms of Sarah’s problem behavior with increases in Luvox.

Bill’s indirect analysis outcome matched that identified through direct observation for his head-directed self-injury but not for his self-biting, crying and aggression. That is, although staff reported that Abilify was effective in decreasing Bill’s self-biting, the direct observation data showed that it was not. In a similar vein, although staff reported that Abilify did not have a treatment effect on Bill’s aggression and self-biting, his direct observation data indicated that Abilify did have a suppressive effect on his crying and aggression. The session data matched the daily data for head-directed SIB, aggression and self-biting but did not match the daily data for crying.

Steve’s self-injury was decreased with increases in Abilify but his environmental destruction showed no effect. The indirect analysis reported no effect for both responses. Session data were consistent with findings from the daily data.

Sarah’s SIB and verbal perseveration increased as she was tapered off of Luvox, demonstrating that Luvox had been suppressing the behavior but her ritualistic behavior
did not show any changes when the medication was discontinued. The indirect data matched the daily data by indicating that Luvox had a treatment effect on Sarah’s SIB and had no effect on her ritualistic behavior. However, the indirect analysis did not yield the same outcome as the daily data for Sarah’s verbal perseveration. In addition, Sarah’s session data matched those obtained from her daily data (i.e., both indicated a treatment effect for her SIB, but not for her ritualistic behavior and verbal perseveration).

**Discussion**

The current analysis extends the previous research by evaluating the effects of medication across multiple topographies of behavior and various doses using indirect analysis and two methods of direct analysis. There are several implications of the findings of this study. First, our data suggest that indirect analysis may not be an accurate method of identifying medication effects. Indirect and direct analyses of the behavioral changes following medication tapers and titration agreed in only five of the nine target responses evaluated. These results are consistent with those of Hilme et al. (2006), who found that indirect assessment did not consistently correspond with direct measurement. This finding suggests that indirect assessment should not be used to determine the efficacy of medication.

When analyzing the indirect assessment data, we found that three of four disagreements were false negatives, suggesting that staff were more likely to report that the medication did not have an effect when it did have an effect. We also found that the session data corresponded to daily data for six of the nine target responses. Session data showed treatment effects for Sarah’s ritualistic behavior and verbal perseveration, as well as Bill’s crying when the daily data did not show such effects. This finding is not
consistent with that of Valdovinos et al. (2002), who found consistent outcomes across all sample observations (i.e., no treatment effect of risperidone on problem behavior).

Disagreement between session data and daily data could be the result of inaccurate data collection by the staff, or alternatively, the session data may not have been representative of treatment effects (i.e., behavior may have frequently occurred outside of the session times). Using the daily data as the point of comparison, session data were more accurate in reporting medication effects than indirect assessment. Although session data were not reliable with the daily data for all responses, it was more reliable than the indirect analysis. Using the session data as the point of comparison, the indirect analysis corresponded for three of the nine target responses.

A third finding was that the medication had differential effects across participants and topographies of behavior. Increases in Abilify decreased Steve’s self-injury but not his environmental destruction. Abilify decreased one topography of Bill’s self-injury while the other showed no change. These findings provide further support that medication may have a differential effect across behavioral topographies (Crosland et al., 2003).

Previous studies have suggested that medication may have a selective effect because it changes the relevant establishing operation (Thompson et al., 1994; Thompson & Symons, 1999; Northrup et al., 1997a,b). Medication may differentially select responses maintained by escape from demands by making demands less aversive (Thomson & Symons, 1999) or responses maintained by attention by decreasing the reinforcing value of attention (Northrup et al., 1997a,b). Research also indicates that
risperidone may have a selective effect on SIB versus other forms of problem behavior (Gilbirg & Coleman, 1992; Crosland et al., 2003).

Future researchers should aim to identify the variables responsible for influencing the efficacy of medication. Research in this area will provide a greater understanding of the behavioral processes underlying the medication and an explanation as to under what conditions we might expect medication to be effective. This will contribute to an individualized, data-driven system of prescription and titration of psychotropic medication.
References


Figure 1. Percentage of staff reporting Abilify had a treatment effect on Bill’s problem behavior.
Figure 2. Frequency of head-directed SIB per day across days and medication dose.
Figure 3. Dose response curves depicting average responses per day across medication phase. Aggression is depicted in the upper left corner, head-directed SIB in the upper right, self-biting in the lower left and crying in the lower right.
Figure 4. Dose response curves depicting average responses per session across medication phase. Aggression is depicted in the upper left corner, head-directed SIB in the upper right, self-biting in the lower left and crying in the lower right.
Figure 5. Dose response curves depicting average responses per day across medication phase. SIB is depicted in the top panel, environmental destruction is depicted in the lower panel.
Figure 6. Dose response curves depicting average responses per session across medication phase. SIB is depicted in the top panel, environmental destruction is depicted in the lower panel.
Figure 7. Percentage of staff reporting Luvox had treatment effect on Sarah’s problem behavior.
Figure 8. Dose response curves depicting average responses per day across medication phase. SIB is depicted in the top panel, verbal perseveration is depicted in the lower left and ritualistic behavior is depicted in the lower panel.
Figure 9. Dose response curves depicting average responses per session across medication phase. SIB is depicted in the top panel, verbal perseveration is depicted in the lower left and ritualistic behavior is depicted in the lower panel.
<table>
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<tr>
<th>PROBLEM BEHAVIOR</th>
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*Table 9.* Summary table depicting the results of each measurement system in reporting treatment effect on problem behavior.